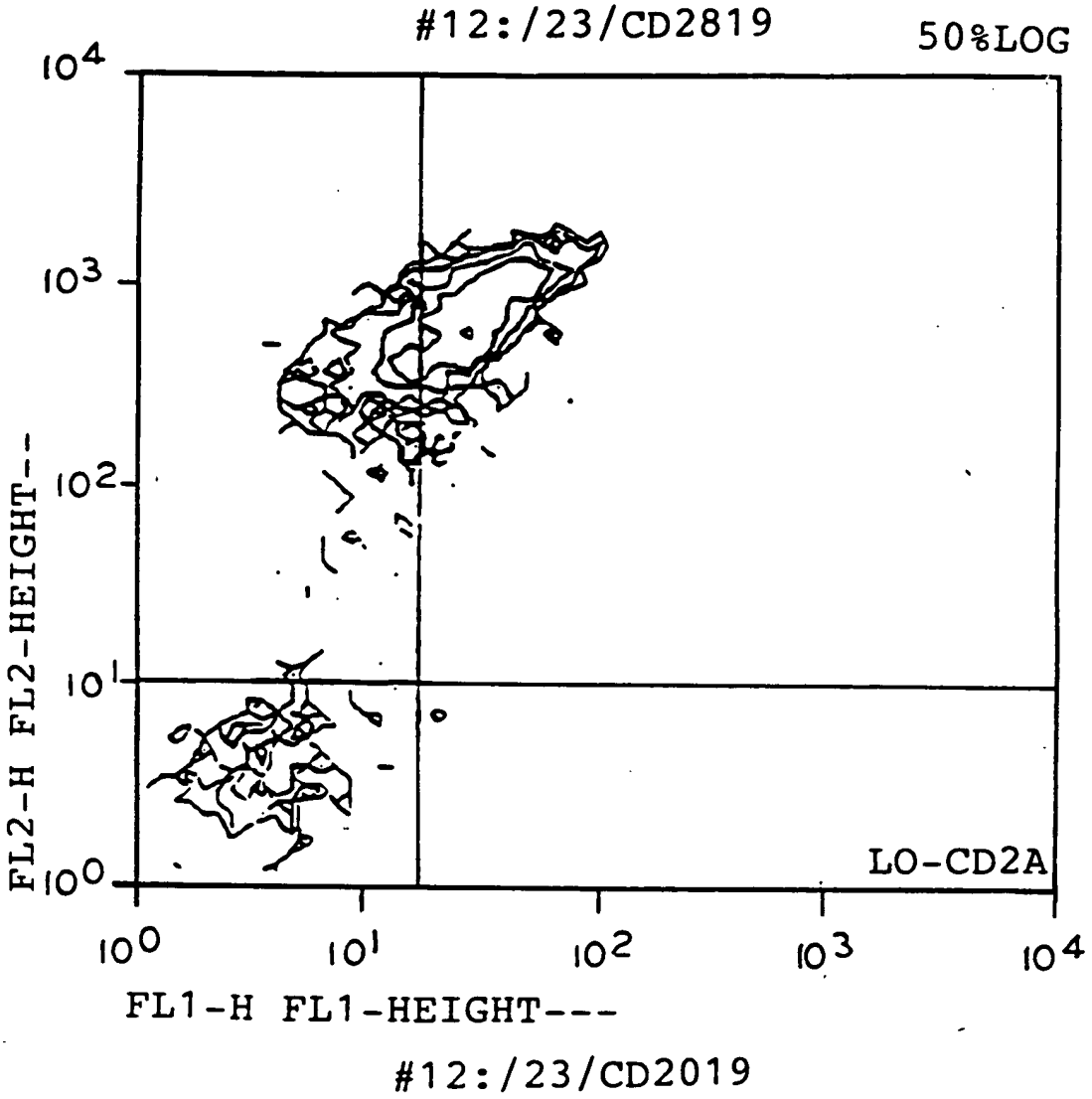
FIG. 1



---QUAD STATS---
FILE: #12:/23/CD2019 SAMPLE: 059
DATE: 9/24/92 GATE G1-R1
PARMETER: FL1-H (LOG) FL2-H(LOG) QUAD
LOCATION:17.15.9

TOTAL= 5000 GATED= L290

QUAD	EVENTS	% GATED	%TOTAL	X MEAN	Y MEAN
IUL	299	23.18	3.98	11.41	284.69
2UR	851	65.97	17.02	32.70	630.65
3LL	135	10.47	2.70	4.08	3.31
4LR	5	0.39	0.10	25.11	6.54

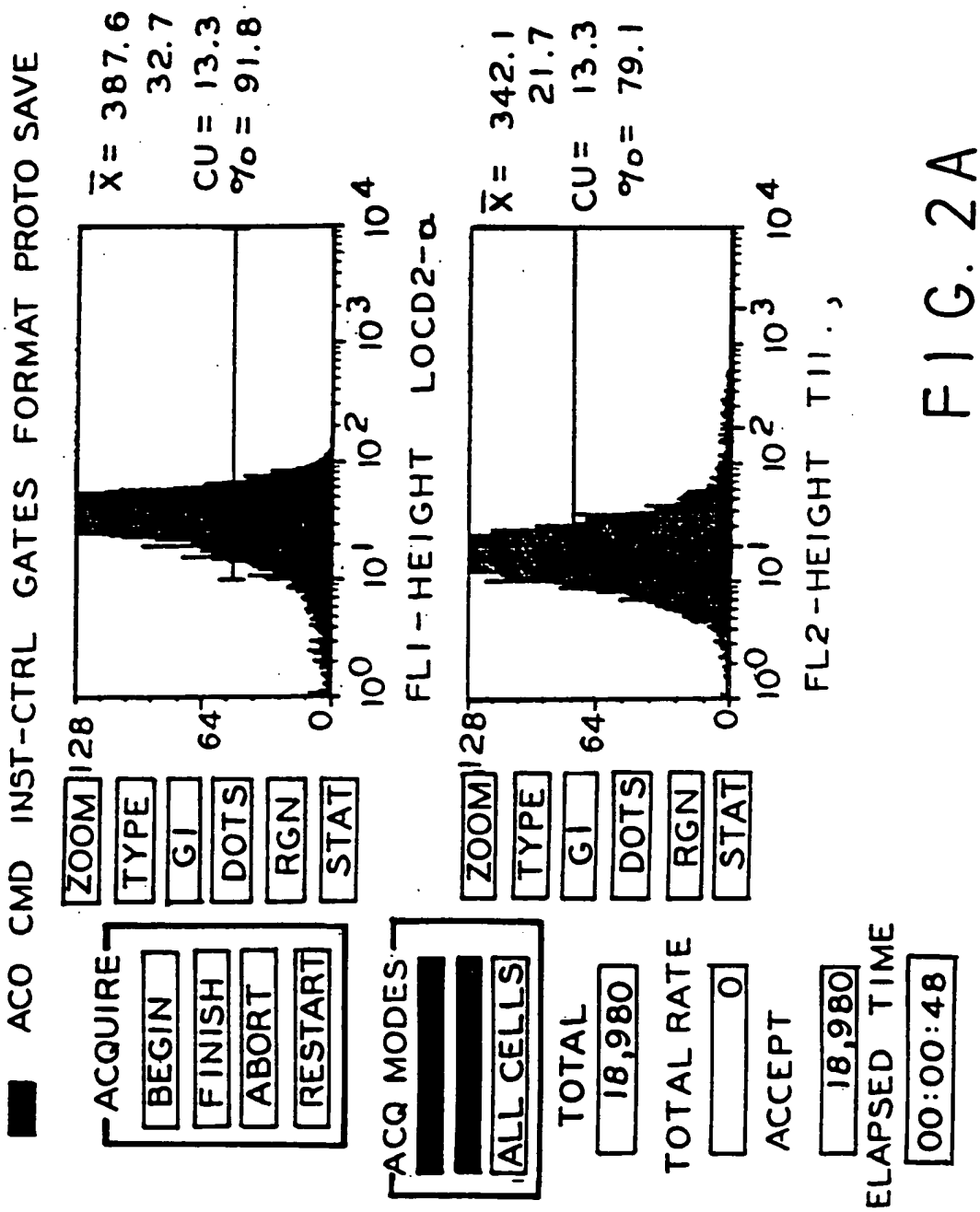

ACO CMD INST-CTRL GATES FORMAT PROTO SAVE
ACQUIRE
BEGIN
FINISH
ABORT
RESTART
ACQ MODES
ALL CELLS
TOTAL
18,980
TOTAL RATE
0
ACCEPT
18,980
ELAPSED TIME
00:00:48
ZOOM
TYPE
GI
DOTS
RGN
STAT
128
64
0
10^0 10^1 10^2 10^3 10^4
FL1-HEIGHT LOCD2-a
$\bar{X}$= 387.6
32.7
CU = 13.3
%o = 91.8
$\bar{X}$= 342.1
21.7
CU= 13.3
%o= 79.1
FL2-HEIGHT T11..

FIG. 2A

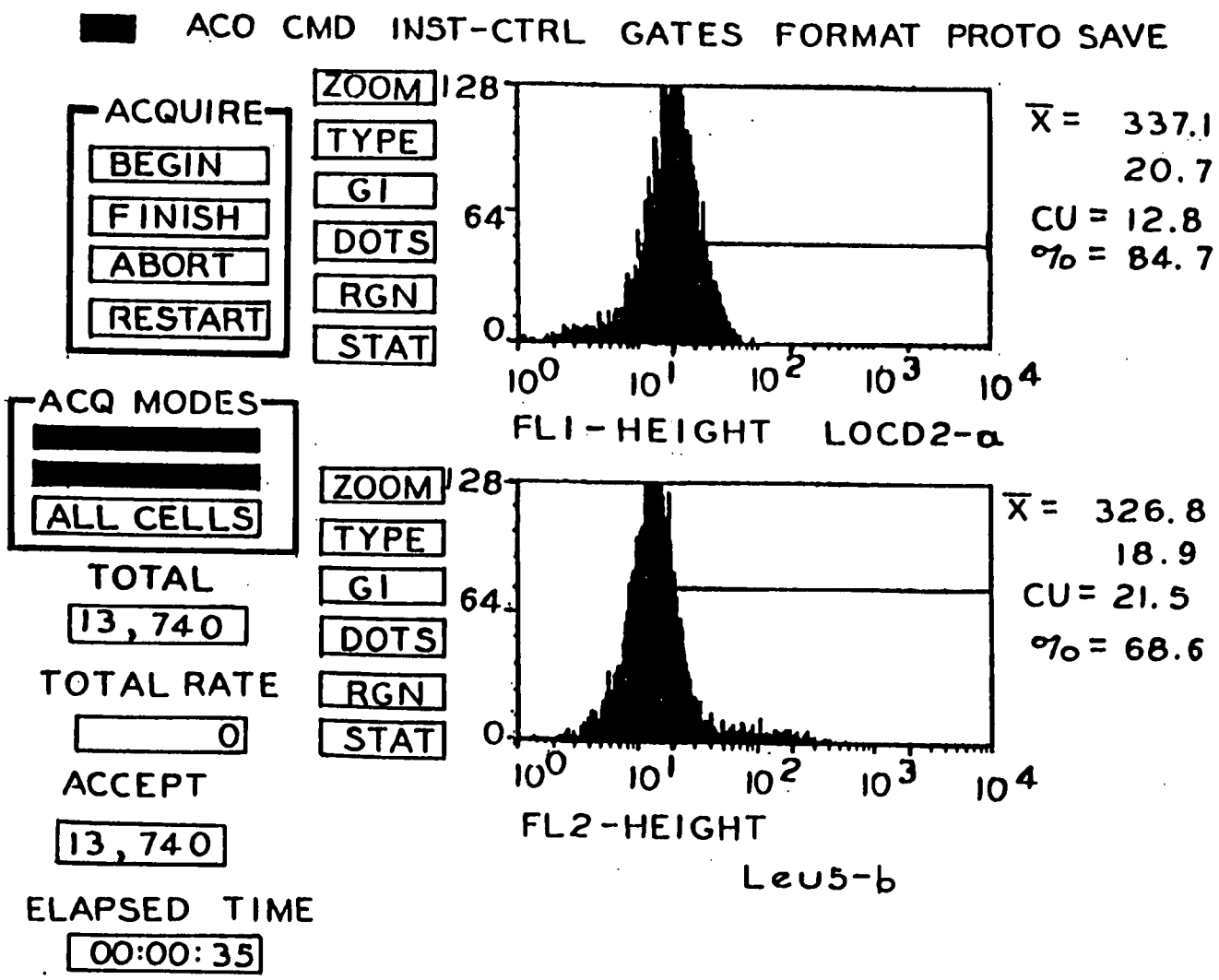

ACO CMD INST-CTRL GATES FORMAT PROTO SAVE
ACQUIRE
BEGIN
FINISH
ABORT
RESTART
ACQ MODES
ALL CELLS
TOTAL
13,740
TOTAL RATE
0
ACCEPT
13,740
ELAPSED TIME
00:00:35
ZOOM
TYPE
GI
DOTS
RGN
STAT
128
64
0
10^0 10^1 10^2 10^3 10^4
FL1-HEIGHT LOCD2-a
$\bar{X}$ = 337.1
20.7
CU = 12.8
% = 84.7
ZOOM
TYPE
GI
DOTS
RGN
STAT
128
64
0
10^0 10^1 10^2 10^3 10^4
FL2-HEIGHT
Leu5-b
$\bar{X}$ = 326.8
18.9
CU = 21.5
% = 68.6

FIG. 2B

FIG. 3A

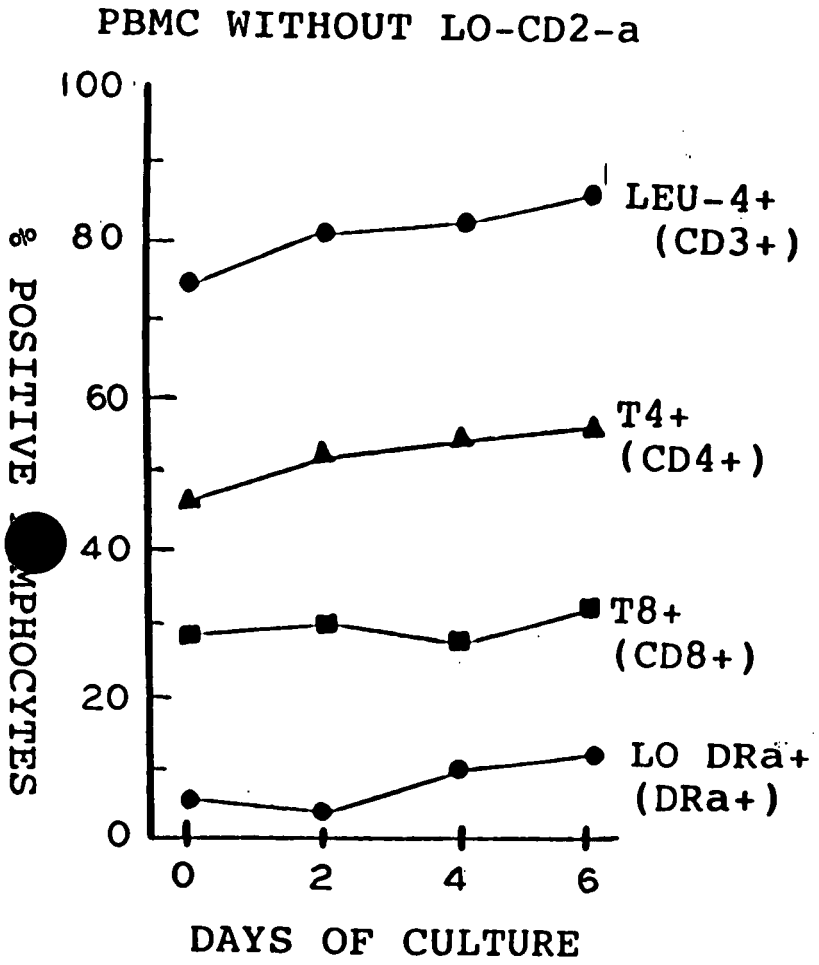

PBMC WITHOUT LO-CD2-a
% POSITIVE LYMPHOCYTES
100
80
60
40
20
0
0
2
4
6
DAYS OF CULTURE
LEU-4+
(CD3+)
T4+
(CD4+)
T8+
(CD8+)
LO DRa+
(DRa+)

FIG. 3B

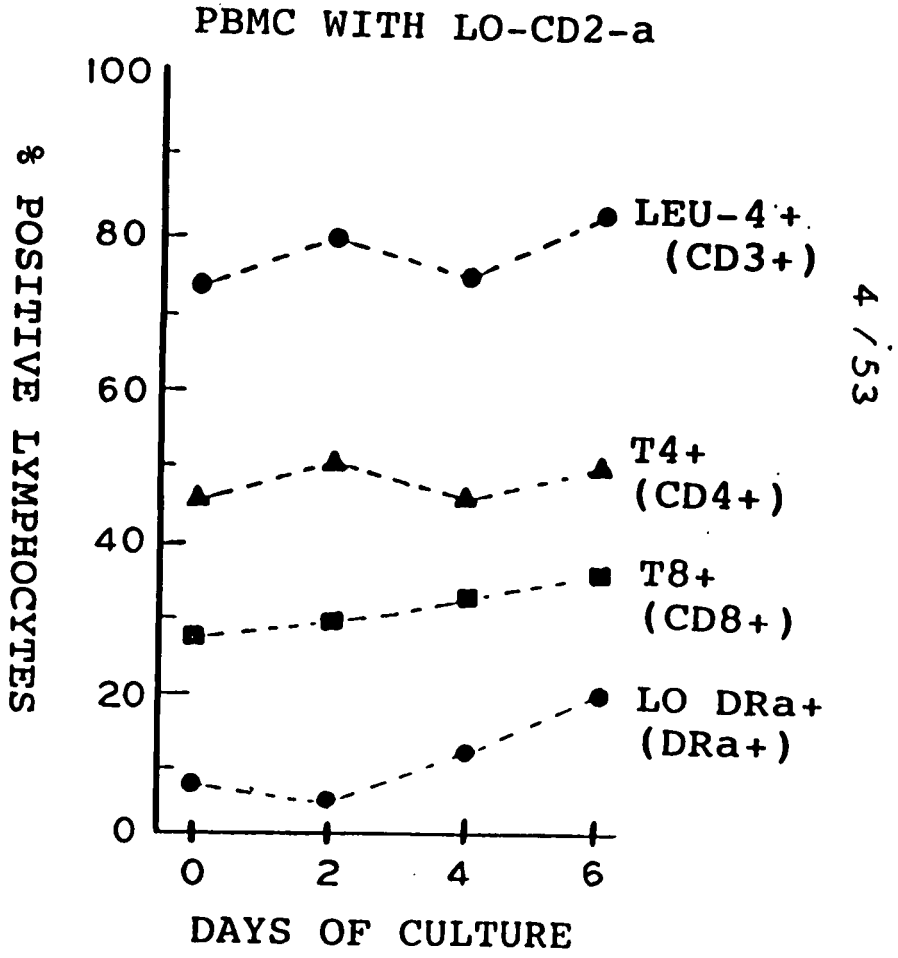

PBMC WITH LO-CD2-a
% POSITIVE LYMPHOCYTES
100
80
60
40
20
0
0
2
4
6
DAYS OF CULTURE
LEU-4+
(CD3+)
T4+
(CD4+)
T8+
(CD8+)
LO DRa+
(DRa+)

FIG. 4

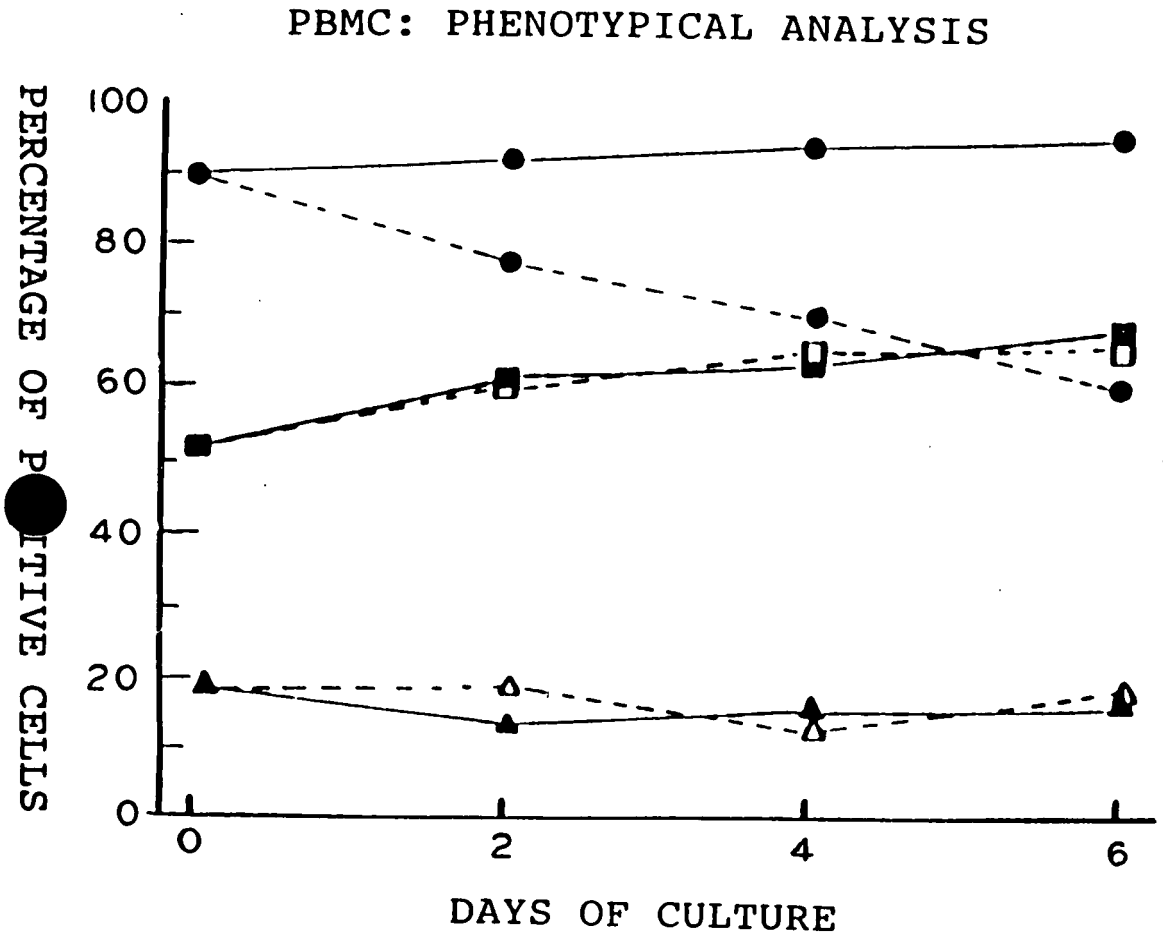

PBMC: PHENOTYPICAL ANALYSIS
PERCENTAGE OF POSITIVE CELLS
100
80
60
40
20
0
0
2
4
6
DAYS OF CULTURE
LEU 5b+ (DC2+)
WITHOUT mAb
WITH mAb
T4+ (CD4+)
WITHOUT mAb
WITH mAb
T8+ (CD8+)
WITHOUT mAb
WITH mAb

FIG. 5A

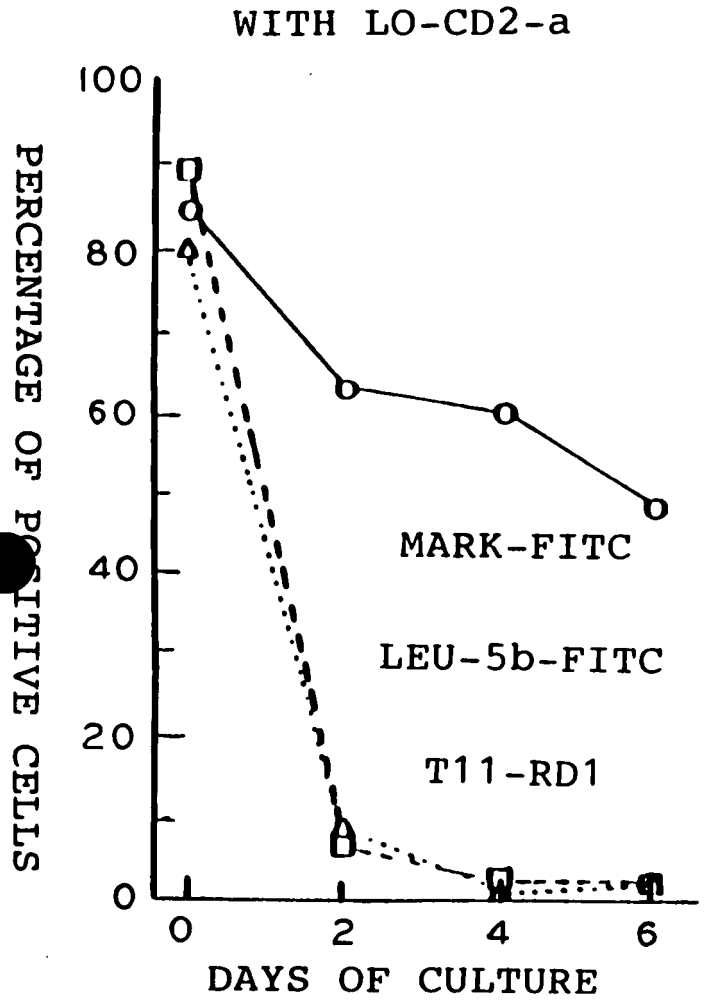
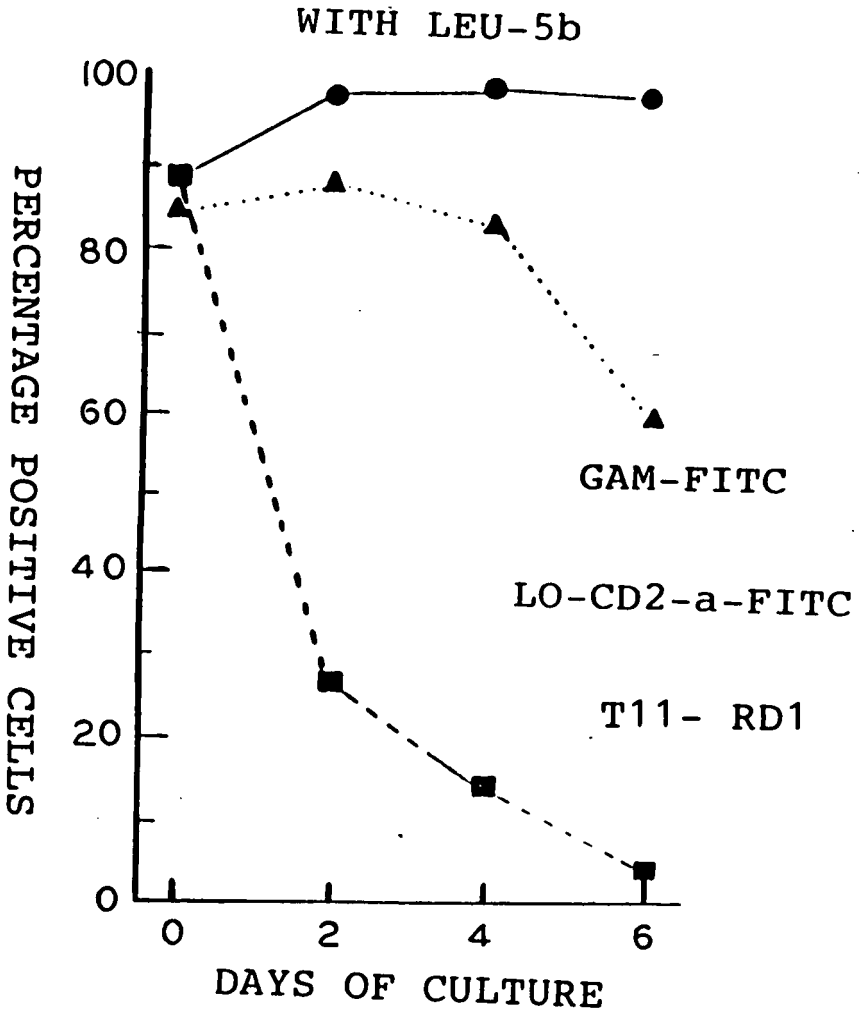

WITH LO-CD2-a
PERCENTAGE OF POSITIVE CELLS
100
80
60
40
20
0
0
2
4
6
DAYS OF CULTURE
MARK-FITC
LEU-5b-FITC
T11-RD1

FIG. 5B


WITH LEU-5b
PERCENTAGE POSITIVE CELLS
100
80
60
40
20
0
0
2
4
6
DAYS OF CULTURE
GAM-FITC
LO-CD2-a-FITC
T11- RD1

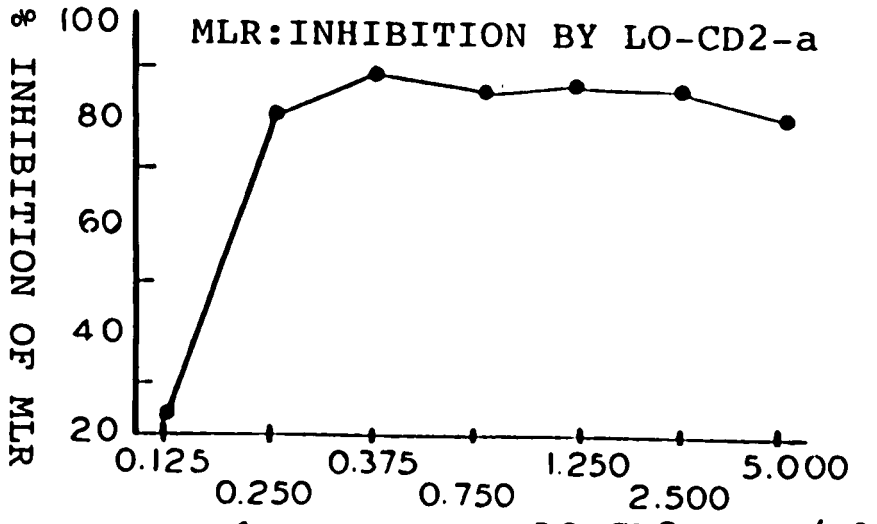


FIG.6A

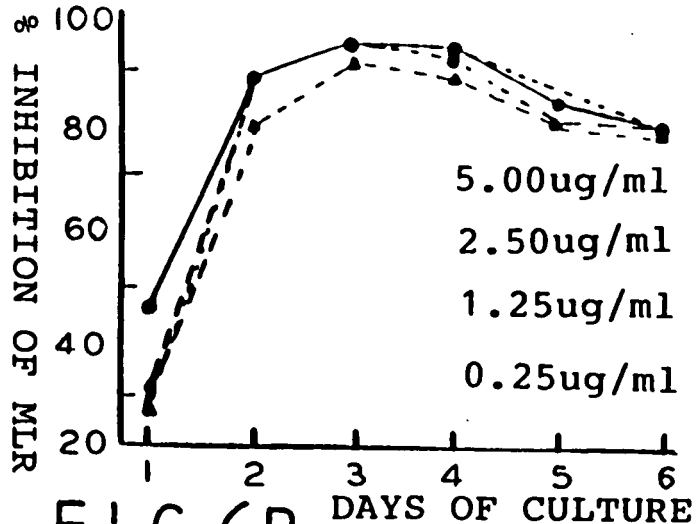


FIG.6B

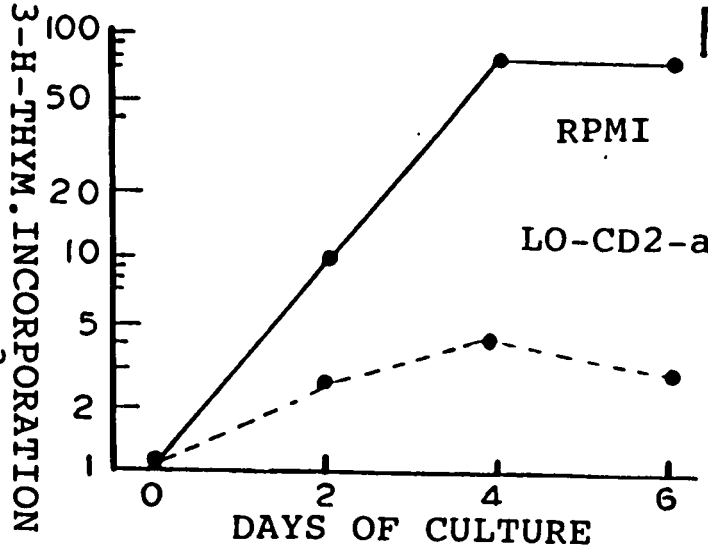


FIG.6C

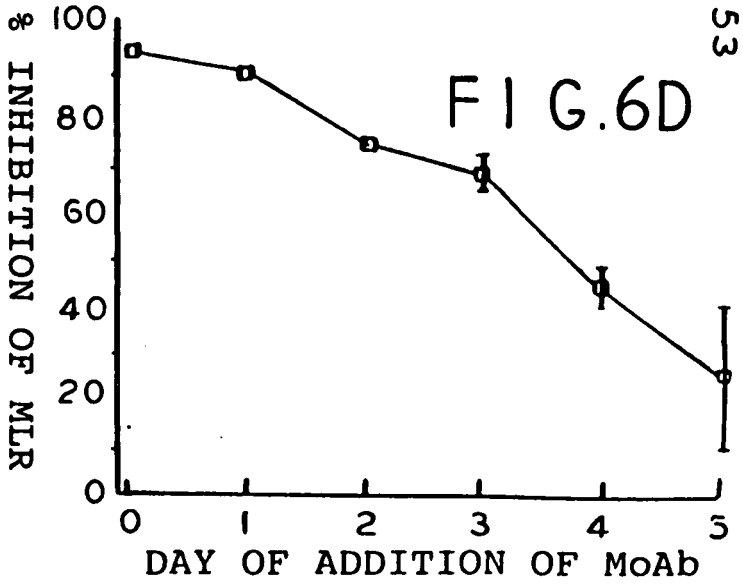


FIG.6D

FIG. 7A

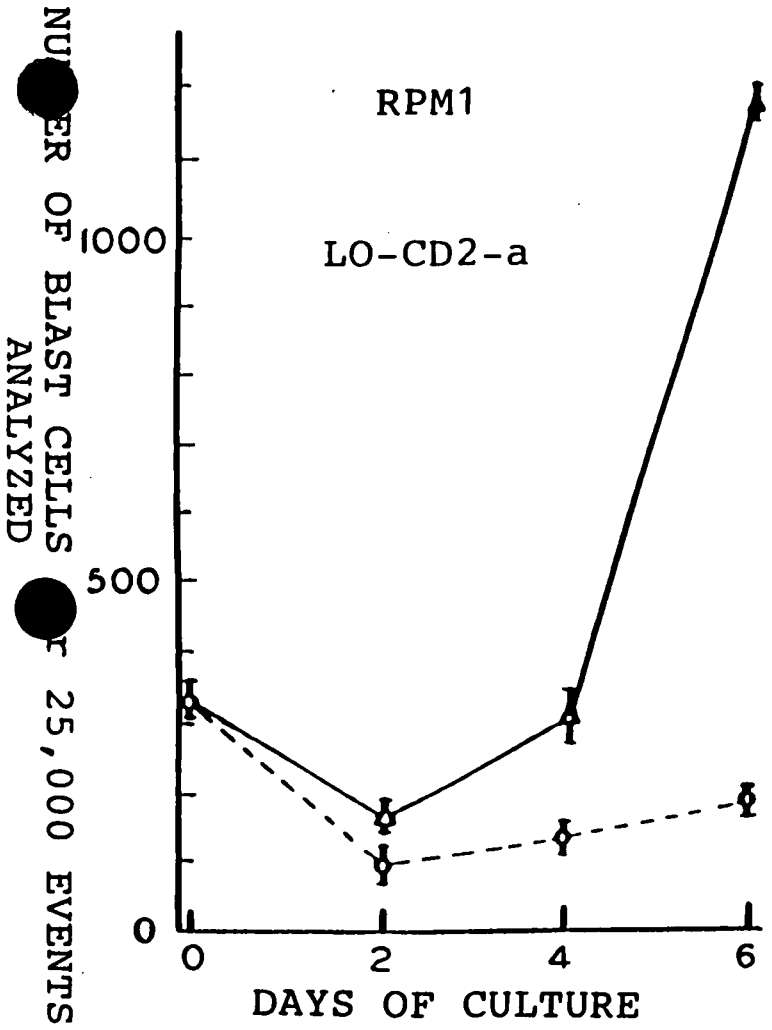

RPM1
LO-CD2-a
NUMBER OF BLAST CELLS IN 25,000 EVENTS ANALYZED
1000
500
0
0
2
4
6
DAYS OF CULTURE

FIG. 7B

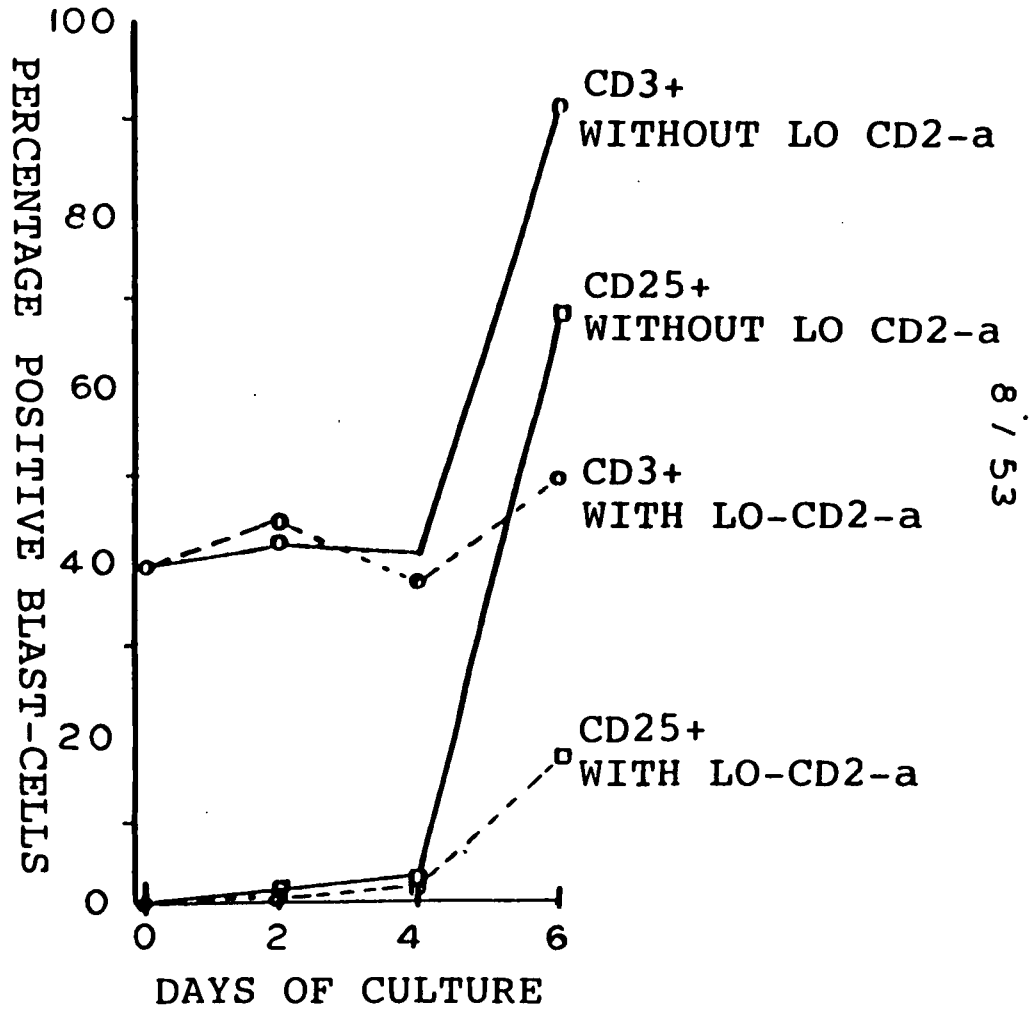
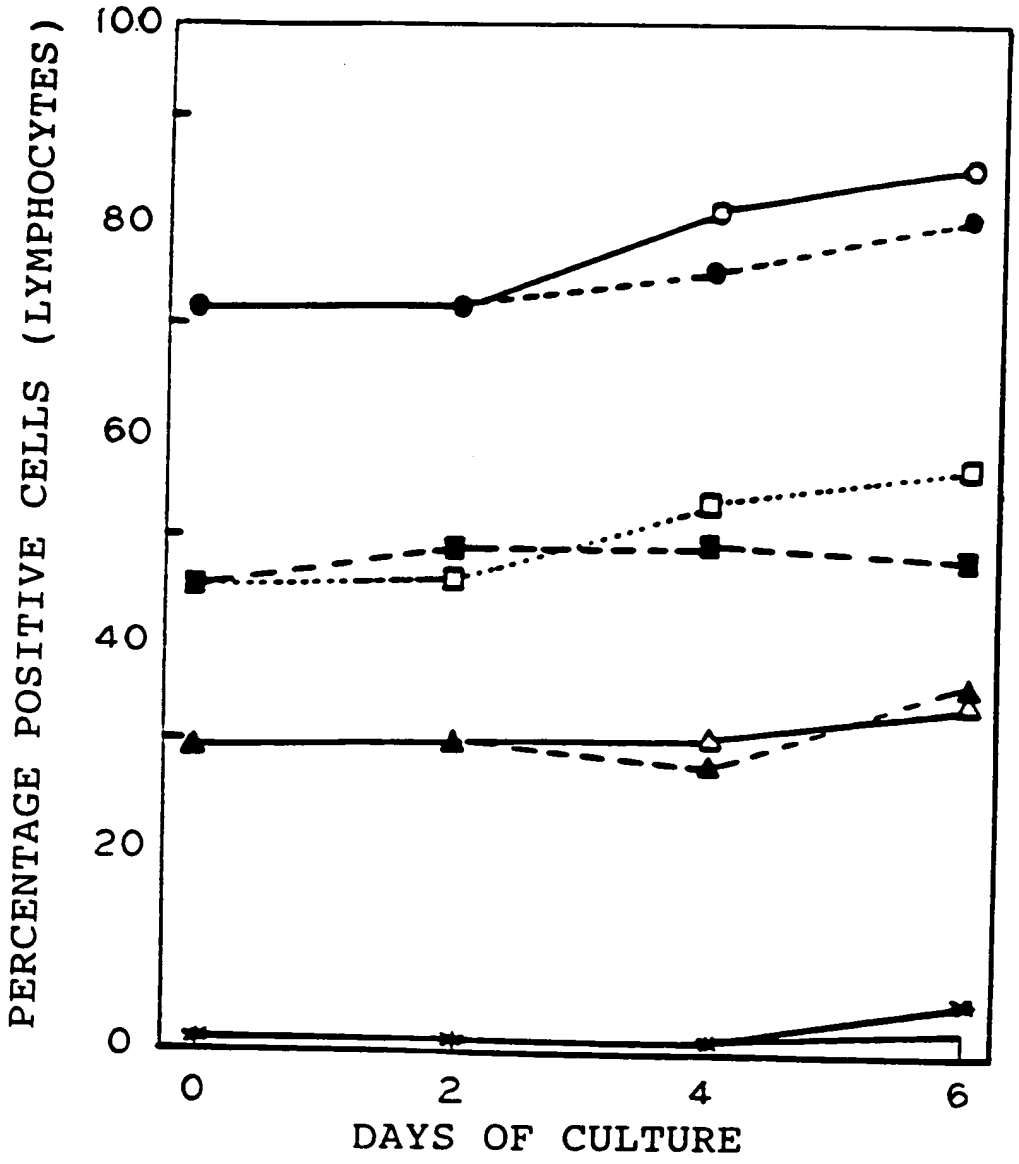

PERCENTAGE POSITIVE BLAST-CELLS
100
80
60
40
20
0
CD3+
WITHOUT LO CD2-a
CD25+
WITHOUT LO CD2-a
CD3+
WITH LO-CD2-a
CD25+
WITH LO-CD2-a
0
2
4
6
DAYS OF CULTURE

FIG. 8A



CD3+ (-MoAb) CD3+ (-MoAb)

CD8+ (-MoAb) CD8+ (+MoAb)

CO4+ (-MoAb) CD4+ (-MoAb)

CD25+ (-MoAb) CD25+ (+MoAb)

FIG. 8B

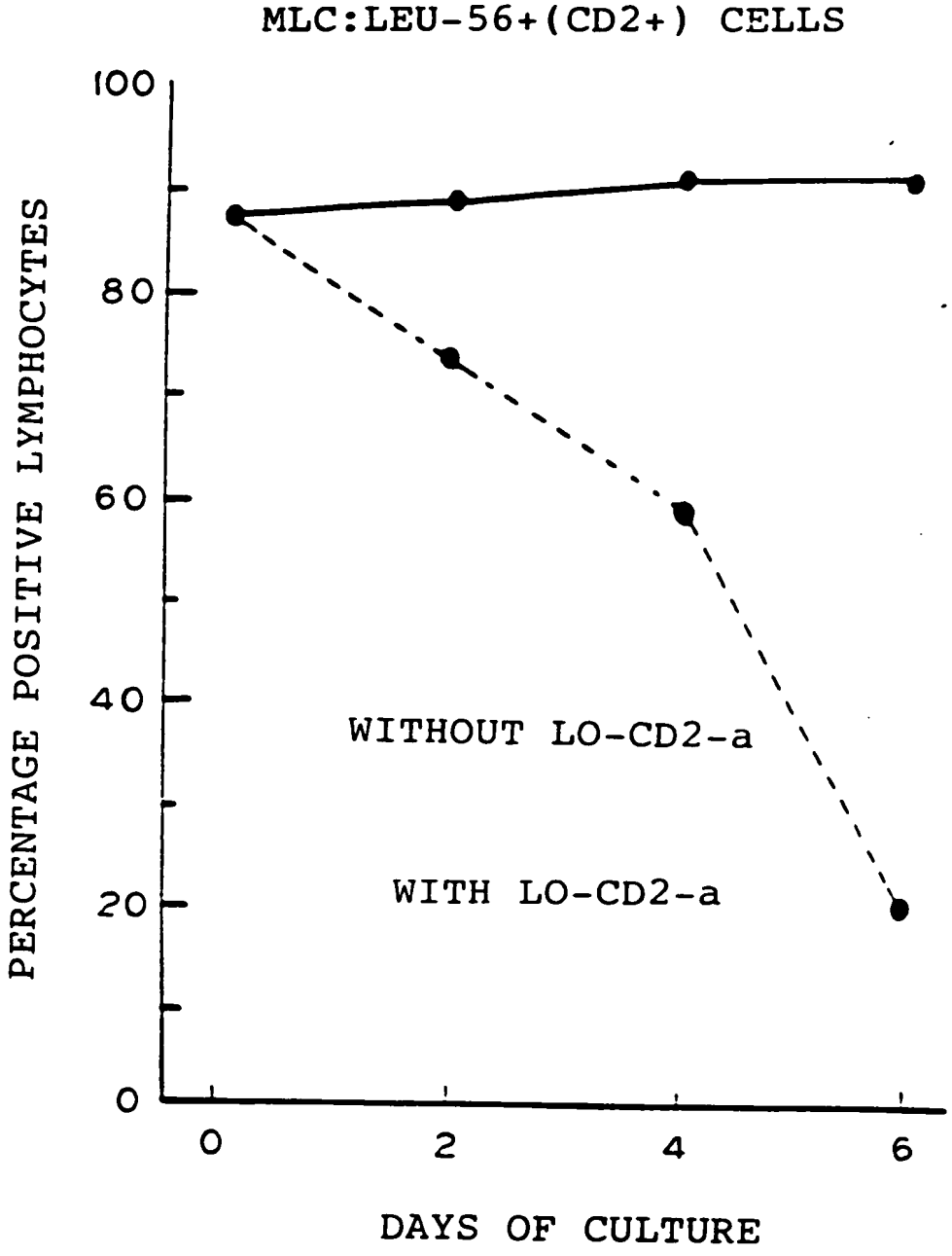


FIG. 9

EFFECTS OF LO-CD2-a ON MITOGEN-STIMULATED PBMC

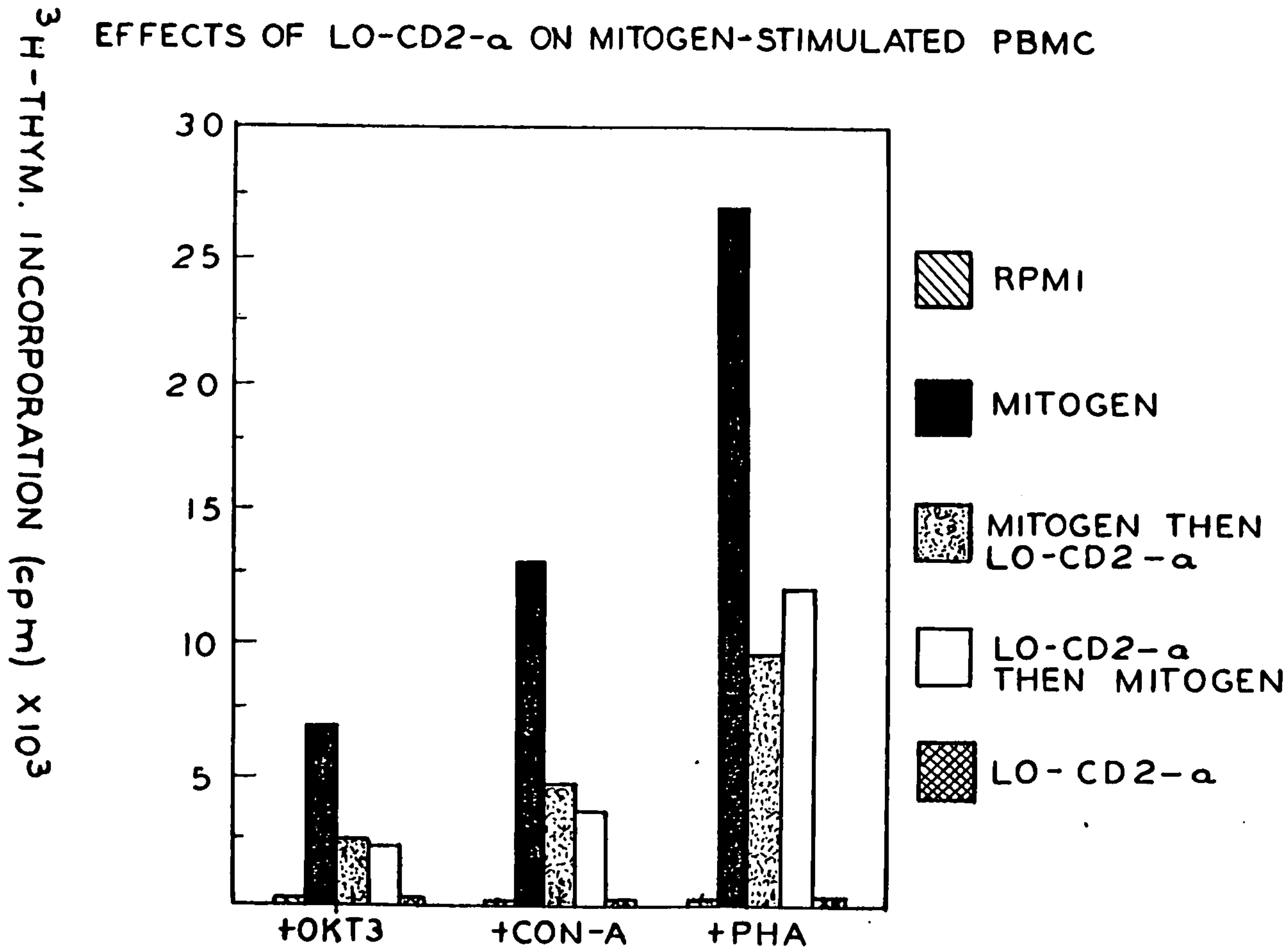


FIG. 10

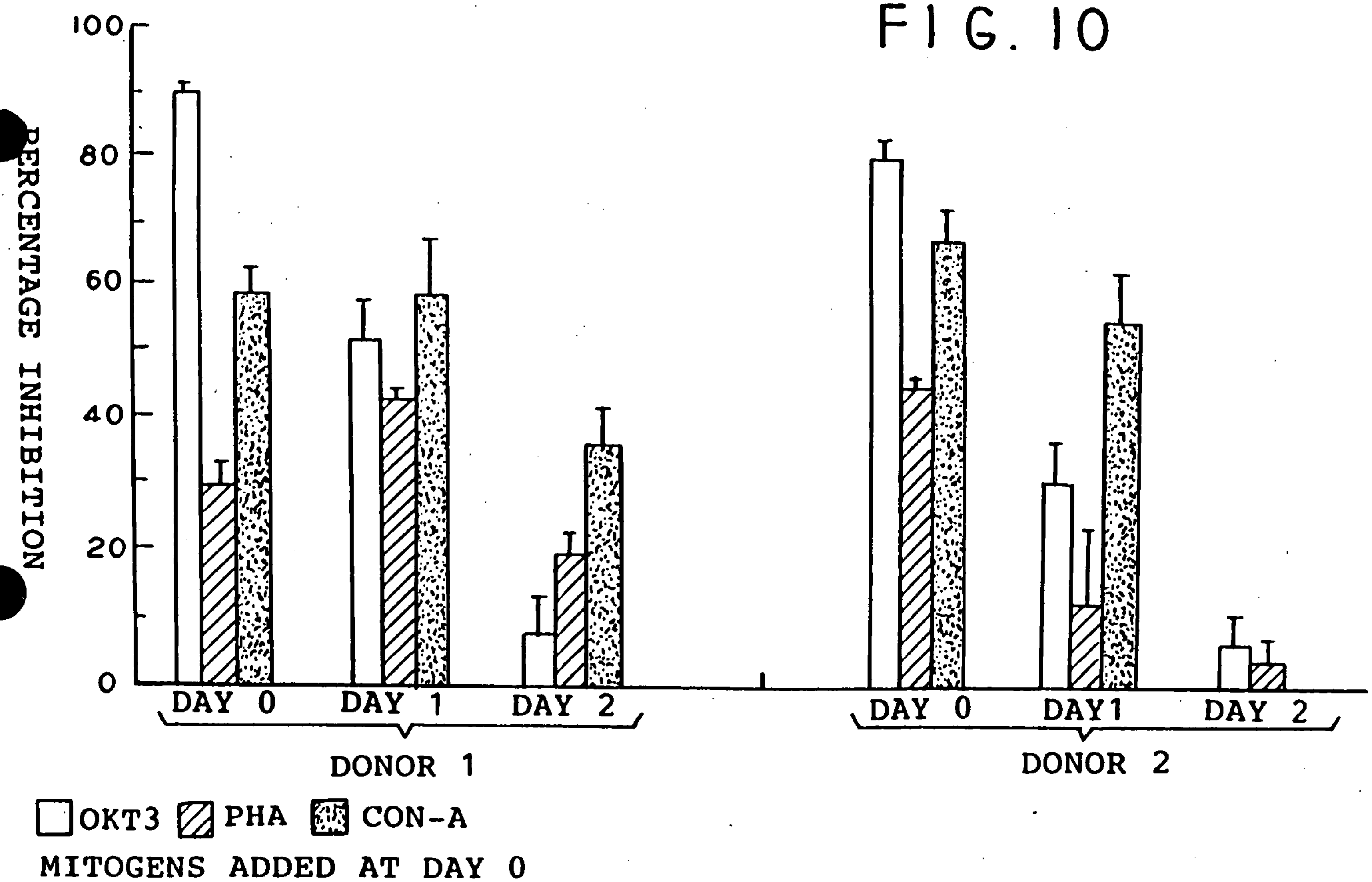

PERCENTAGE INHIBITION
100
80
60
40
20
0
DAY 0
DAY 1
DAY 2
DONOR 1
DAY 0
DAY1
DAY 2
DONOR 2
OKT3
PHA
CON-A
MITOGENS ADDED AT DAY 0

FIG. IIA

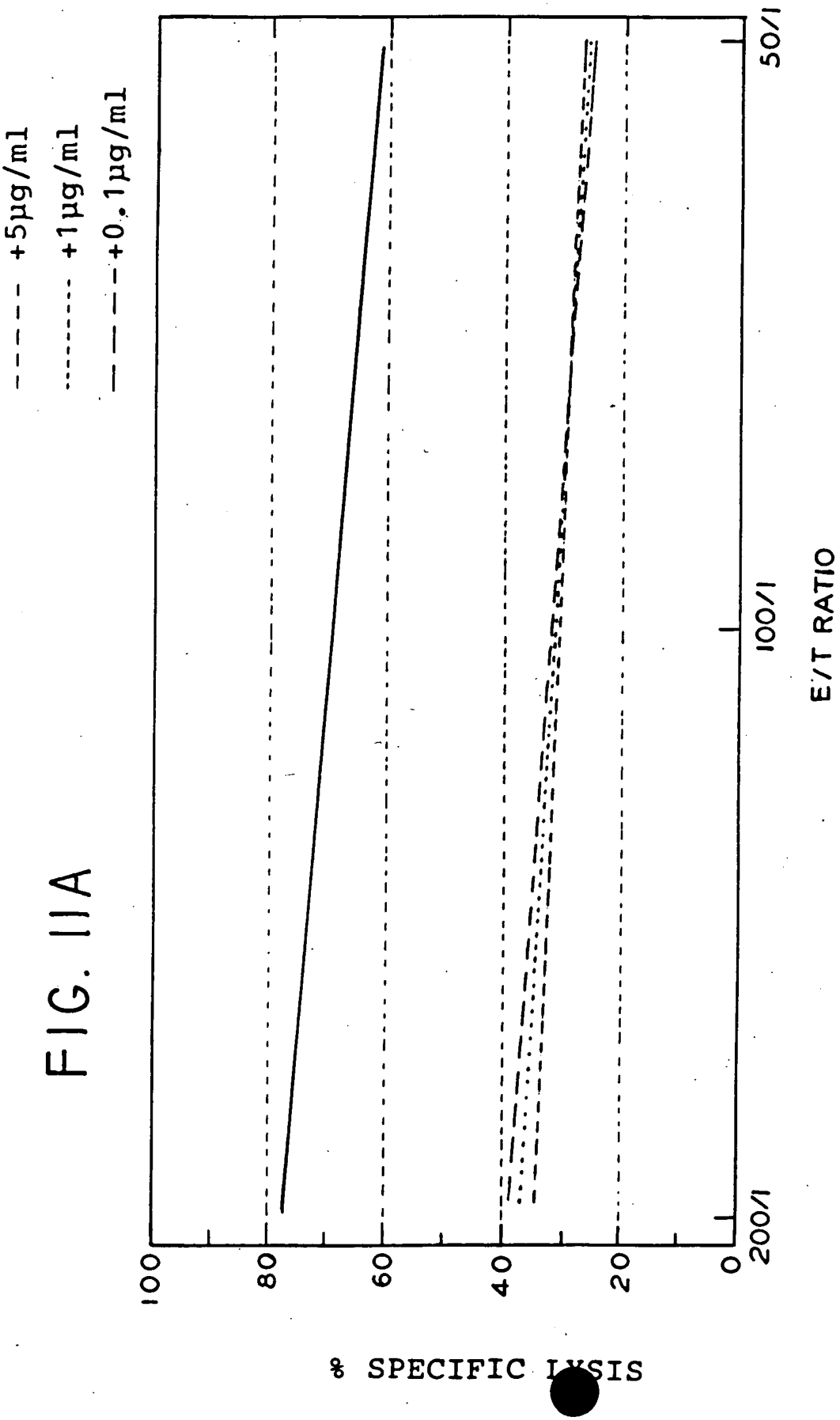


FIG. IIB

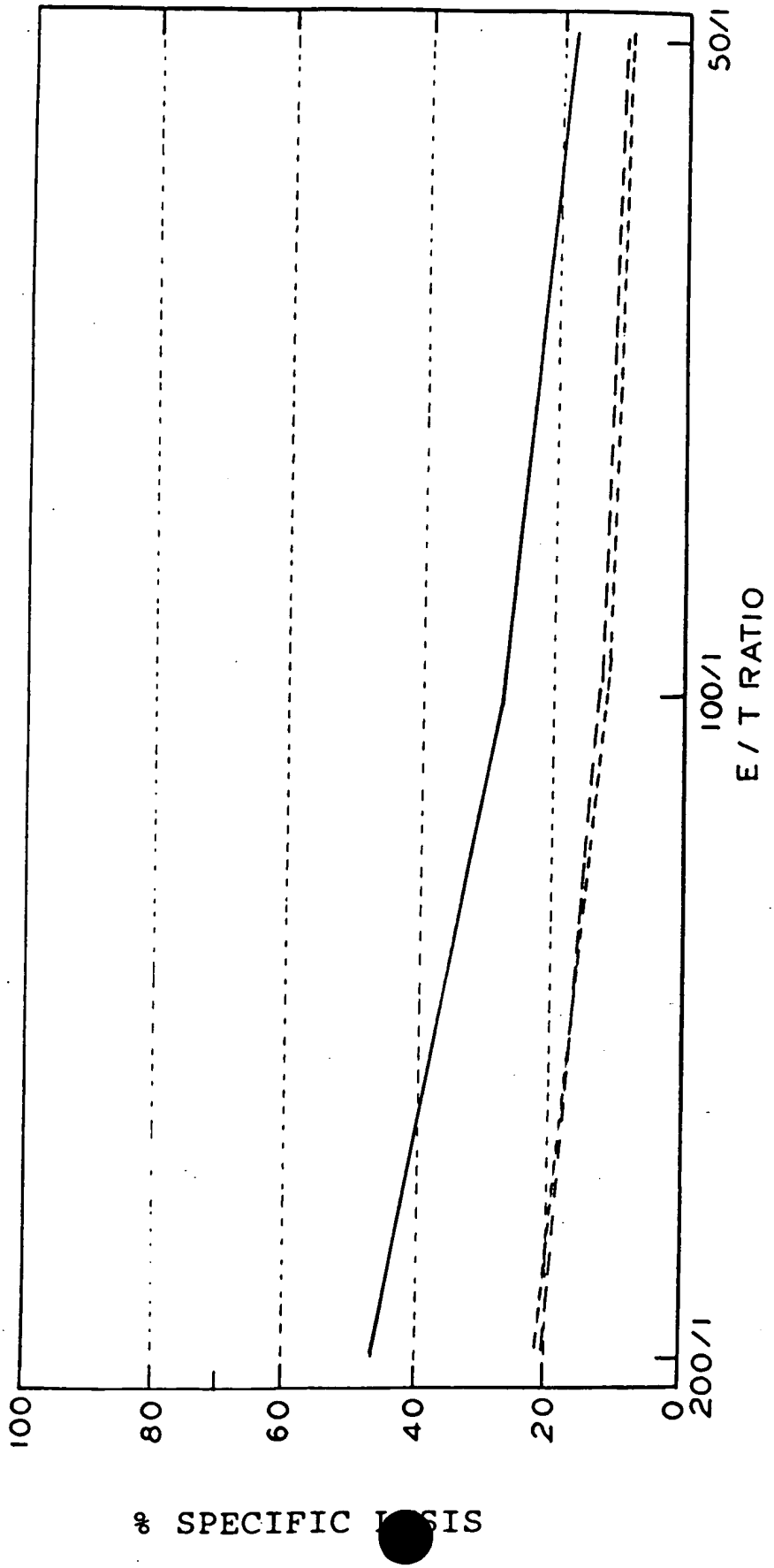


FIG. 12

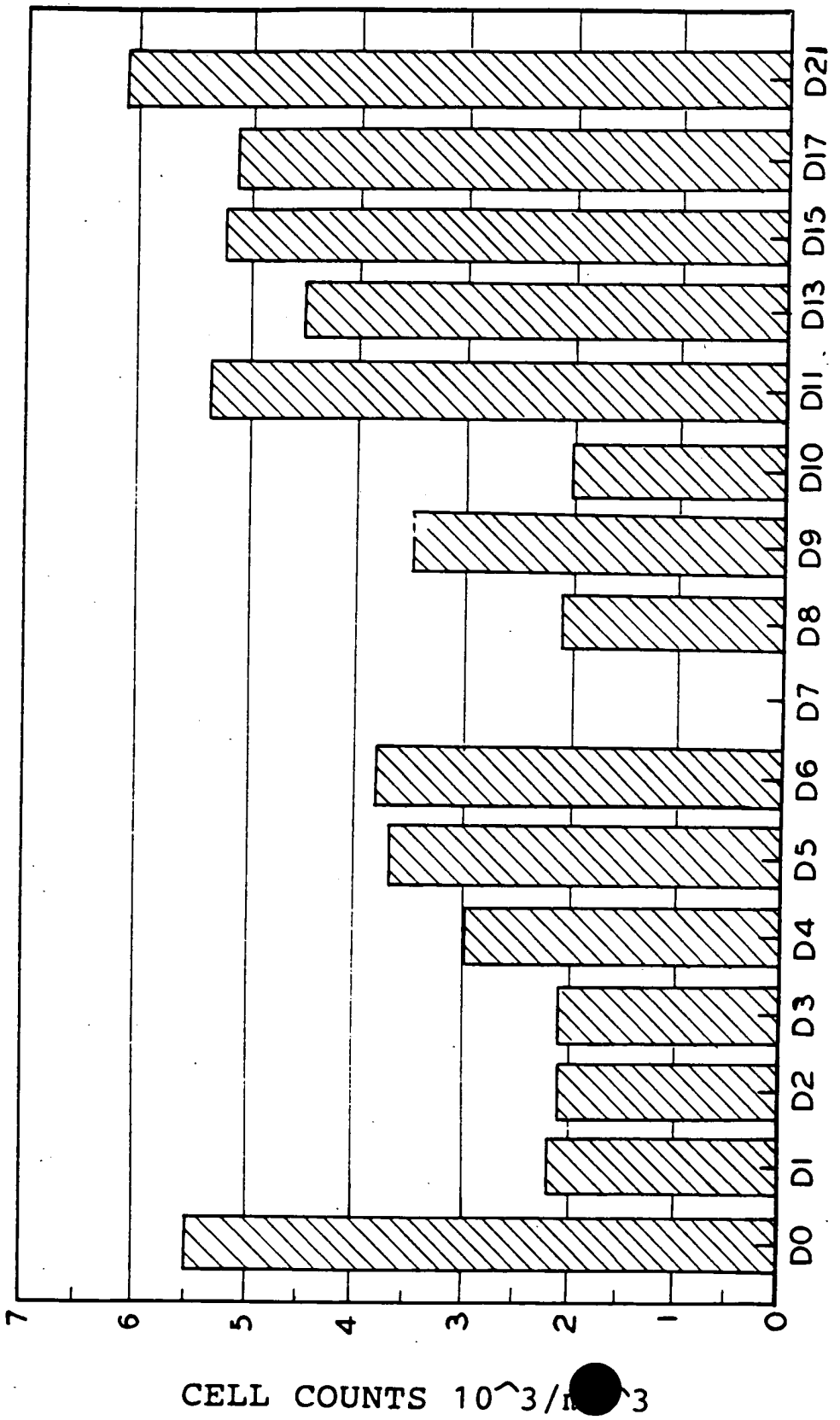


FIG. 13

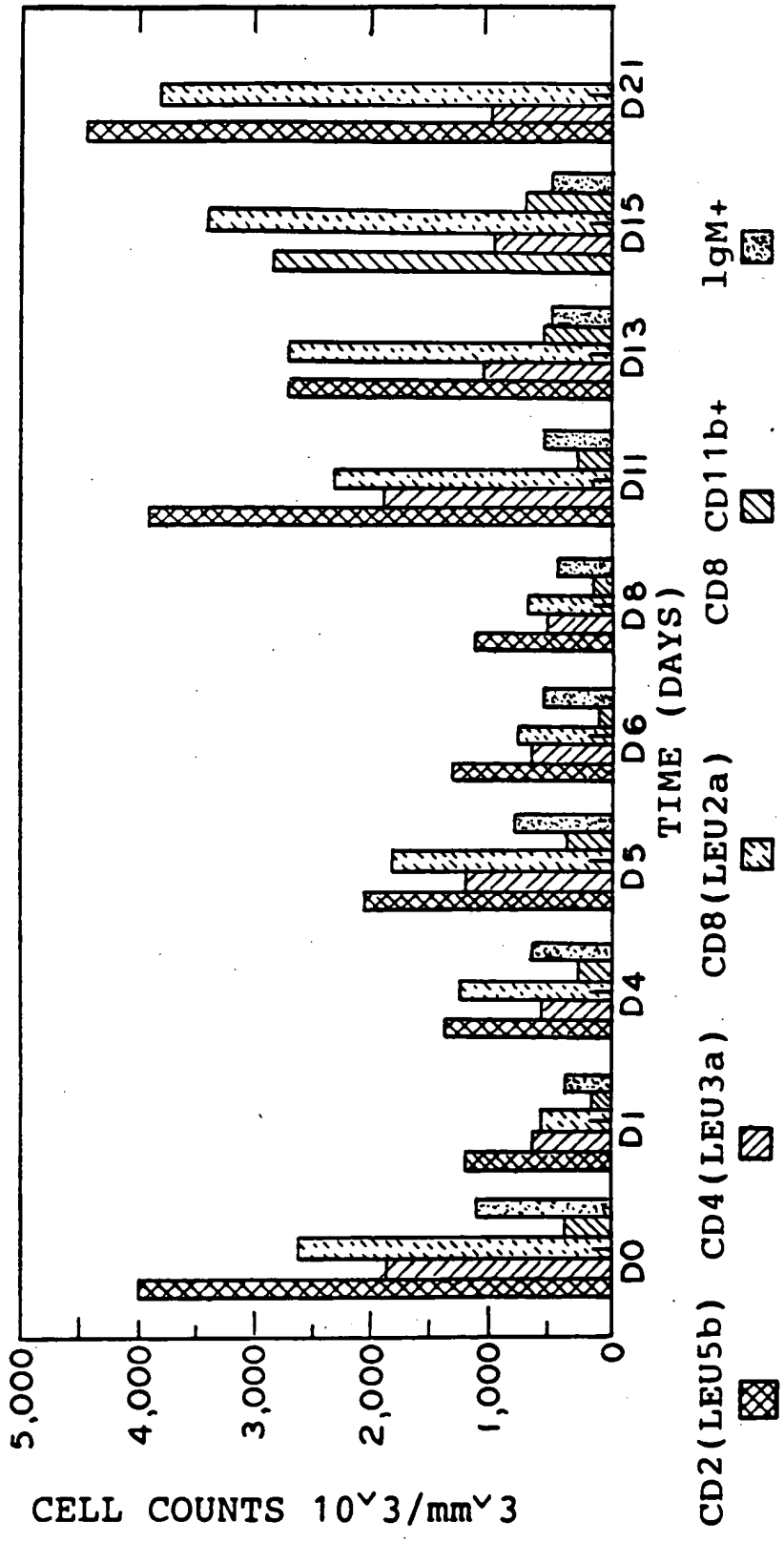


FIG. 14

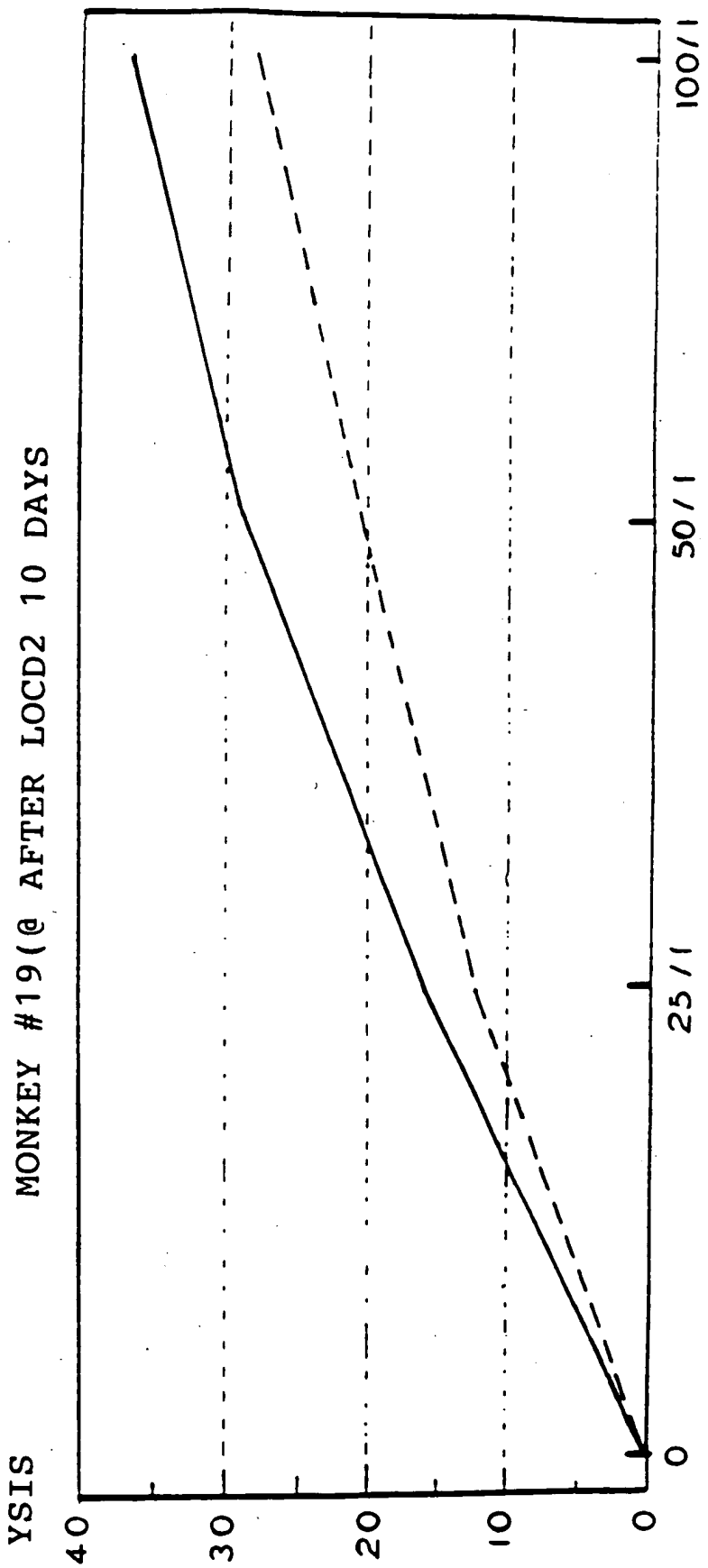


FIG. 15

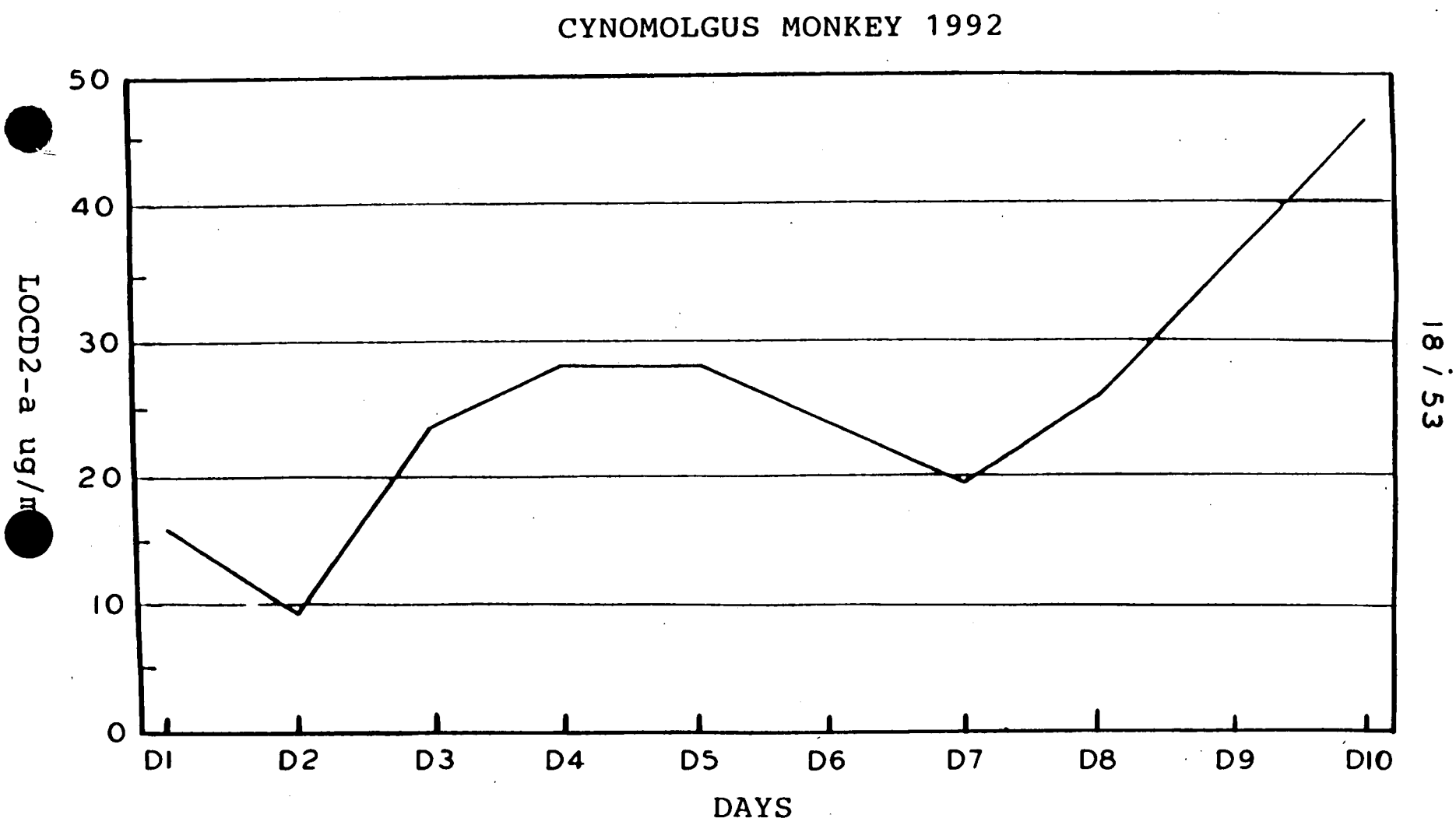

CYNOMOLGUS MONKEY 1992
LOCD2-a ug/m
50
40
30
20
10
0
D1
D2
D3
D4
D5
D6
D7
D8
D9
D10
DAYS

FIG. 16

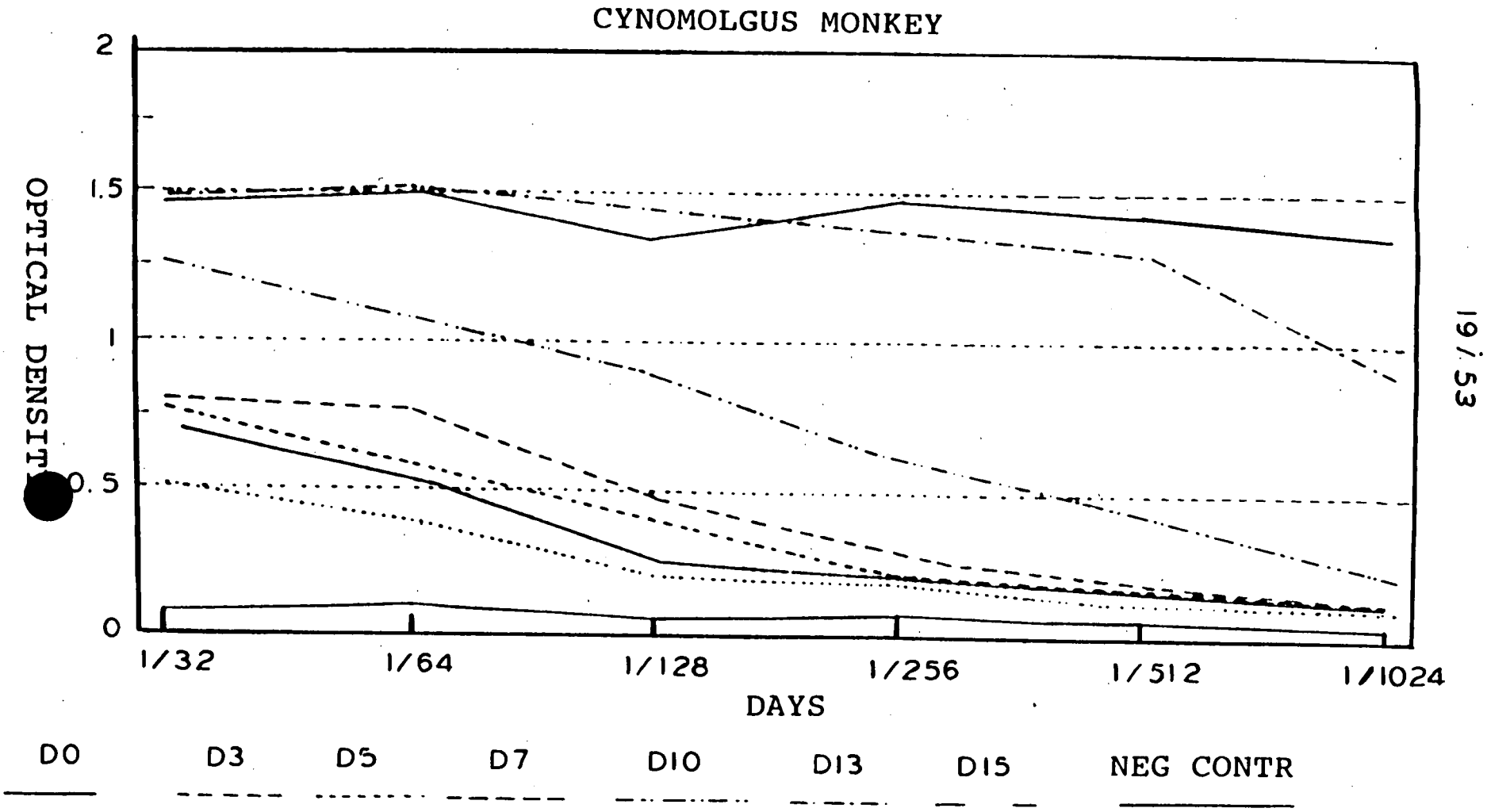

CYNOMOLGUS MONKEY
OPTICAL DENSITY
2
1.5
1
0.5
0
1/32
1/64
1/128
1/256
1/512
1/1024
DAYS
D0
D3
D5
D7
D10
D13
D15
NEG CONTR

FIG. 17A

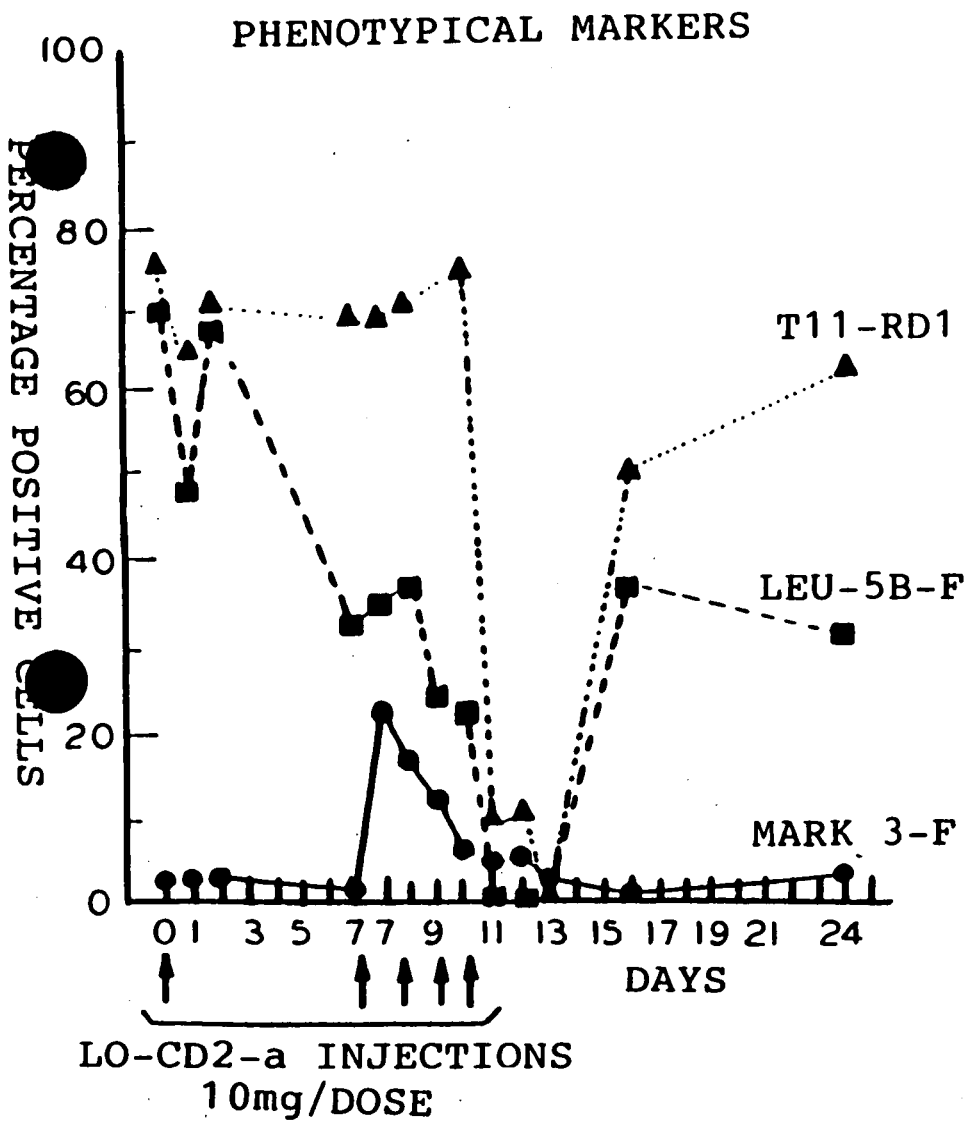


FIG. 17B

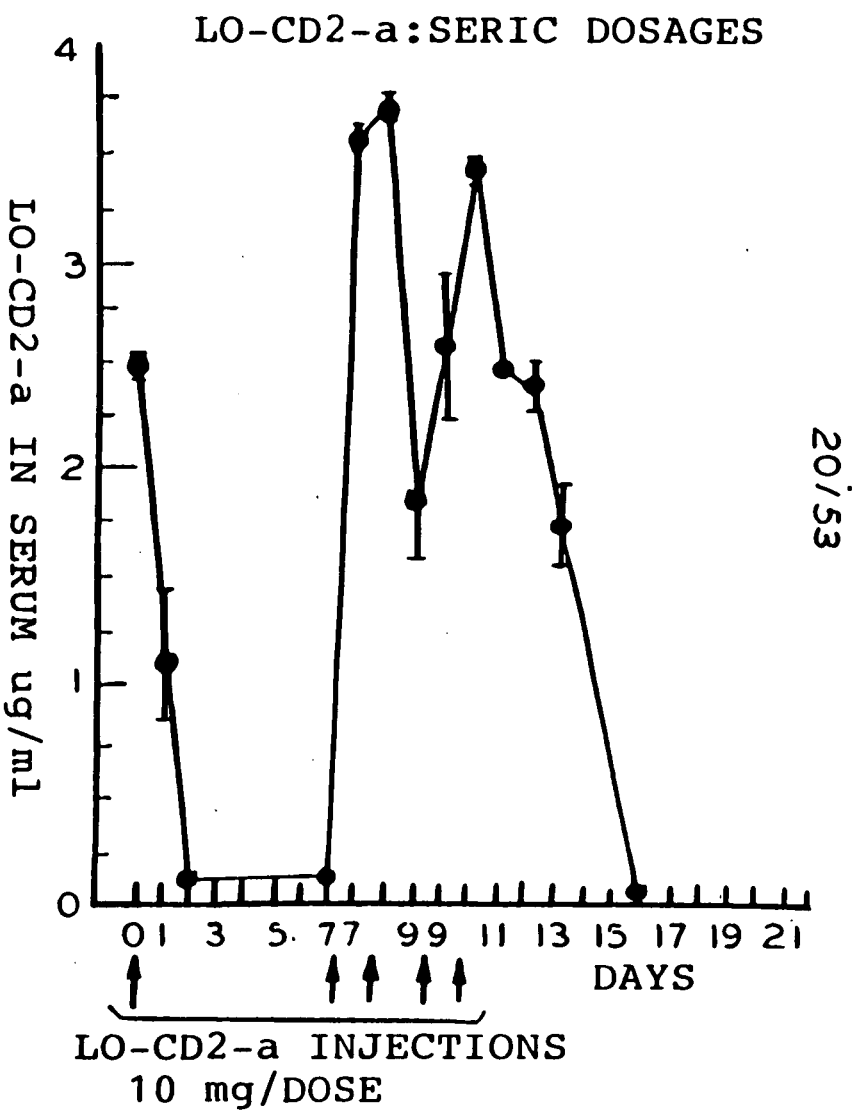


FIG. 18A

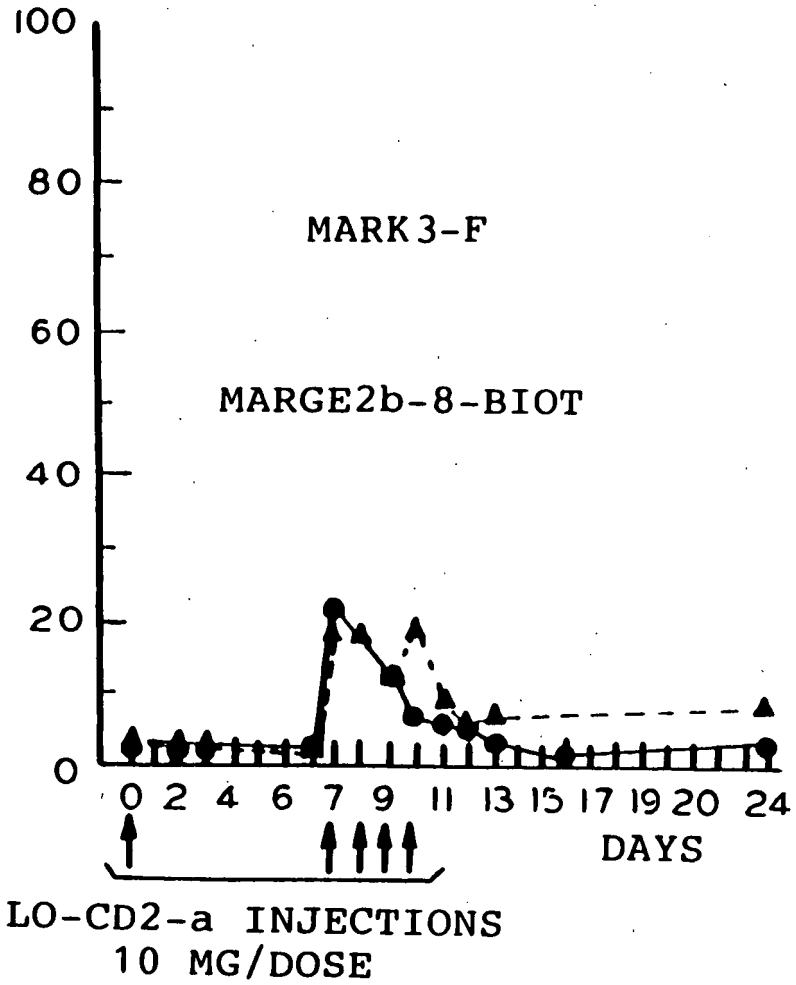


FIG. 18B

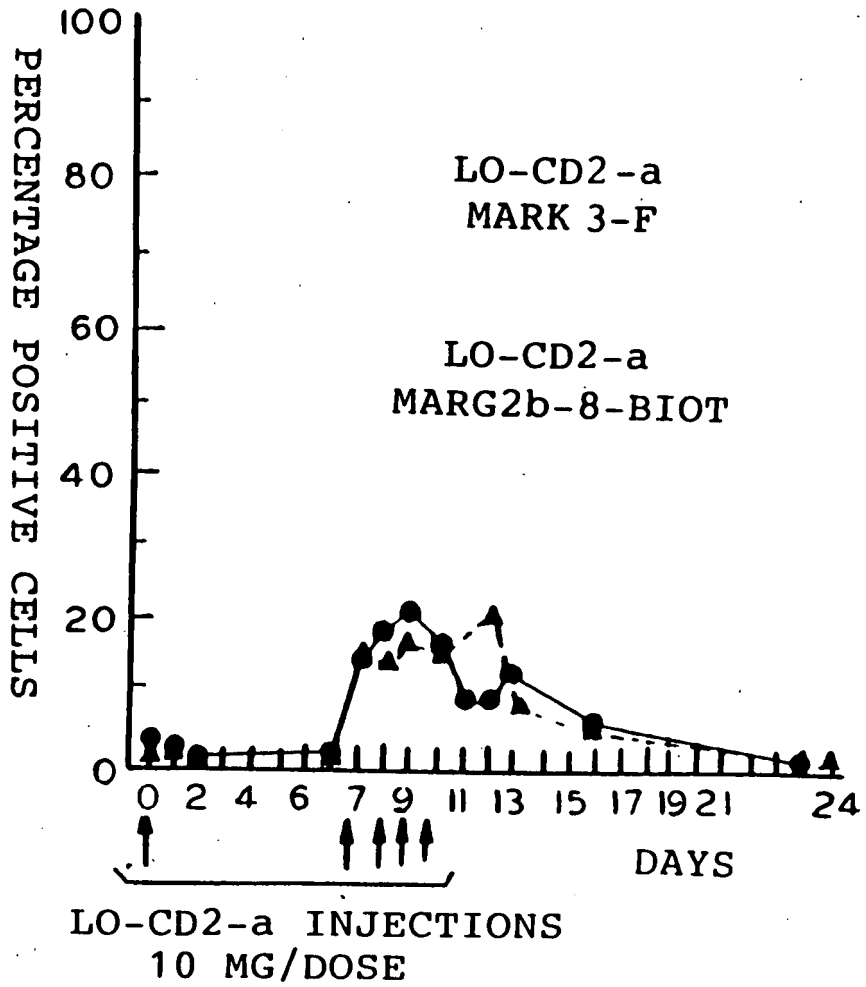


FIG. 19

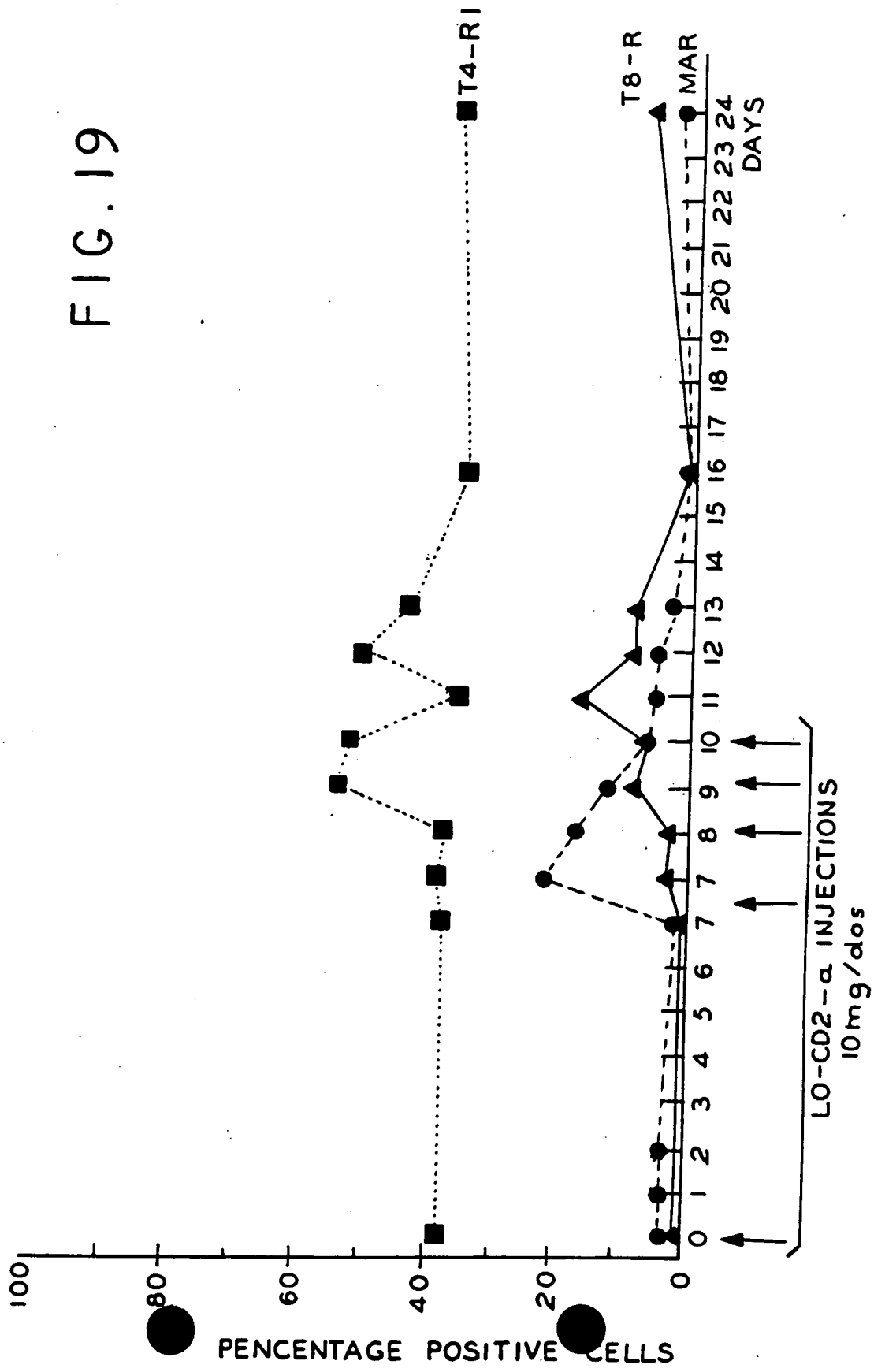


FIG. 20

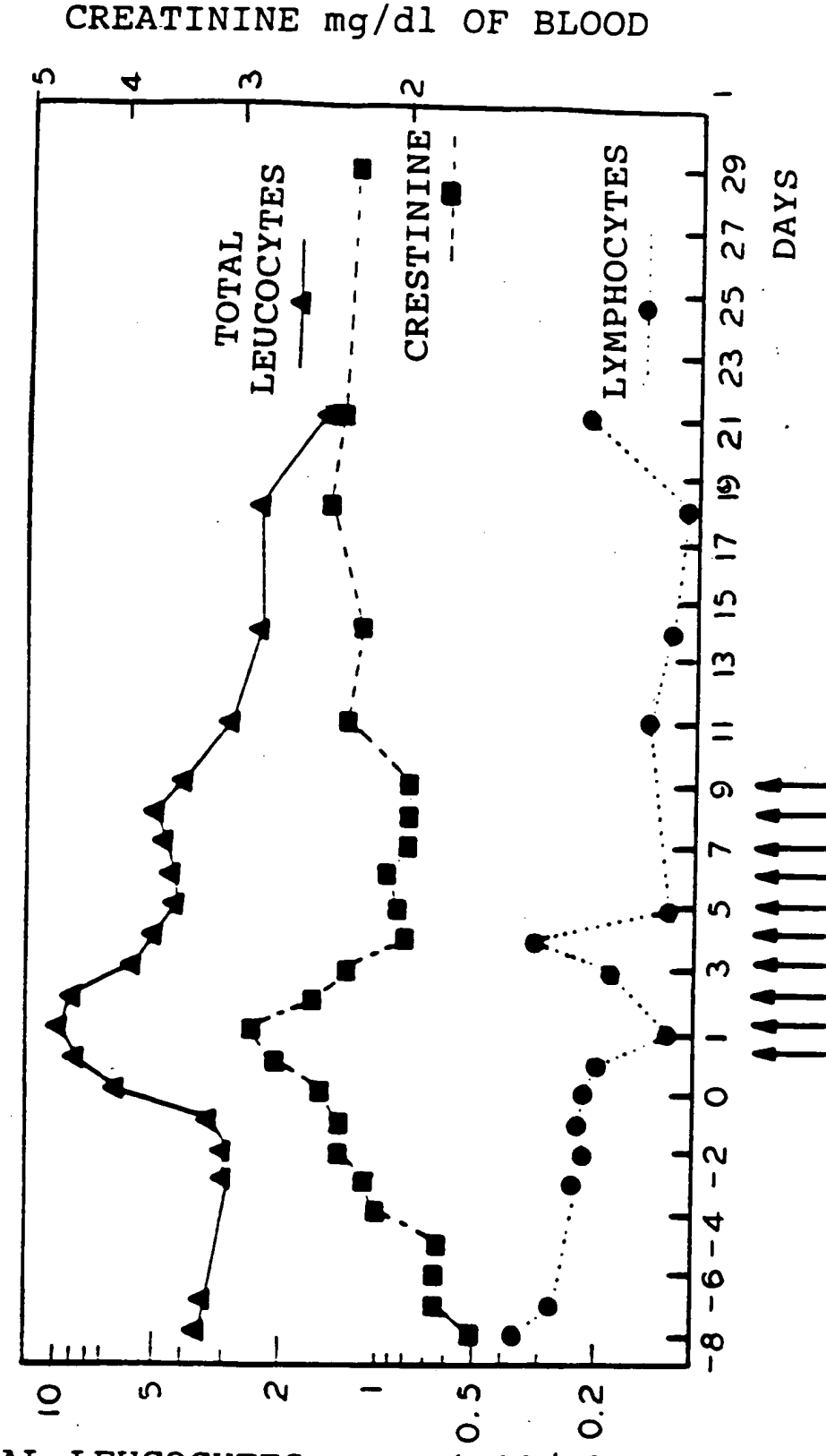
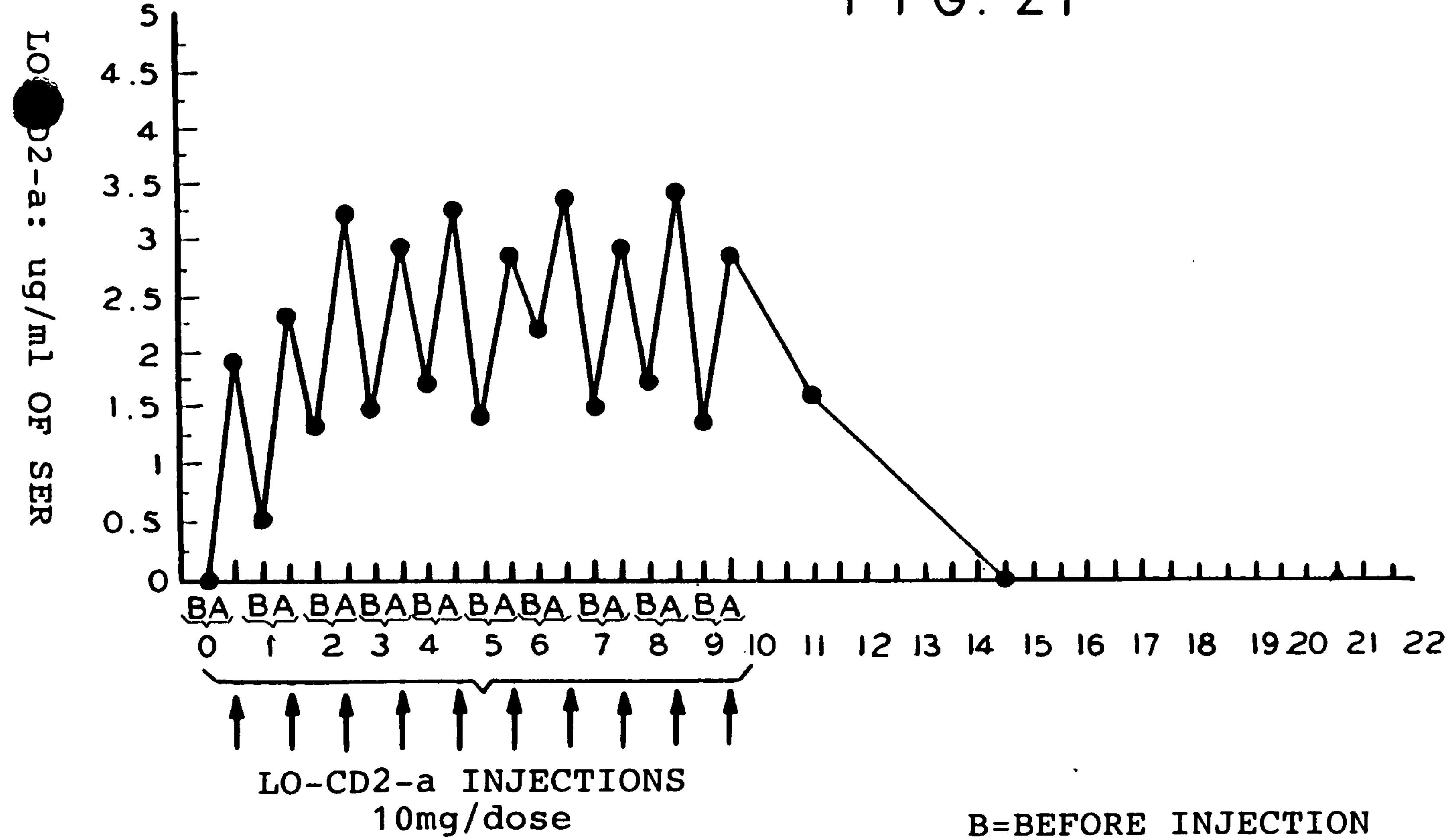
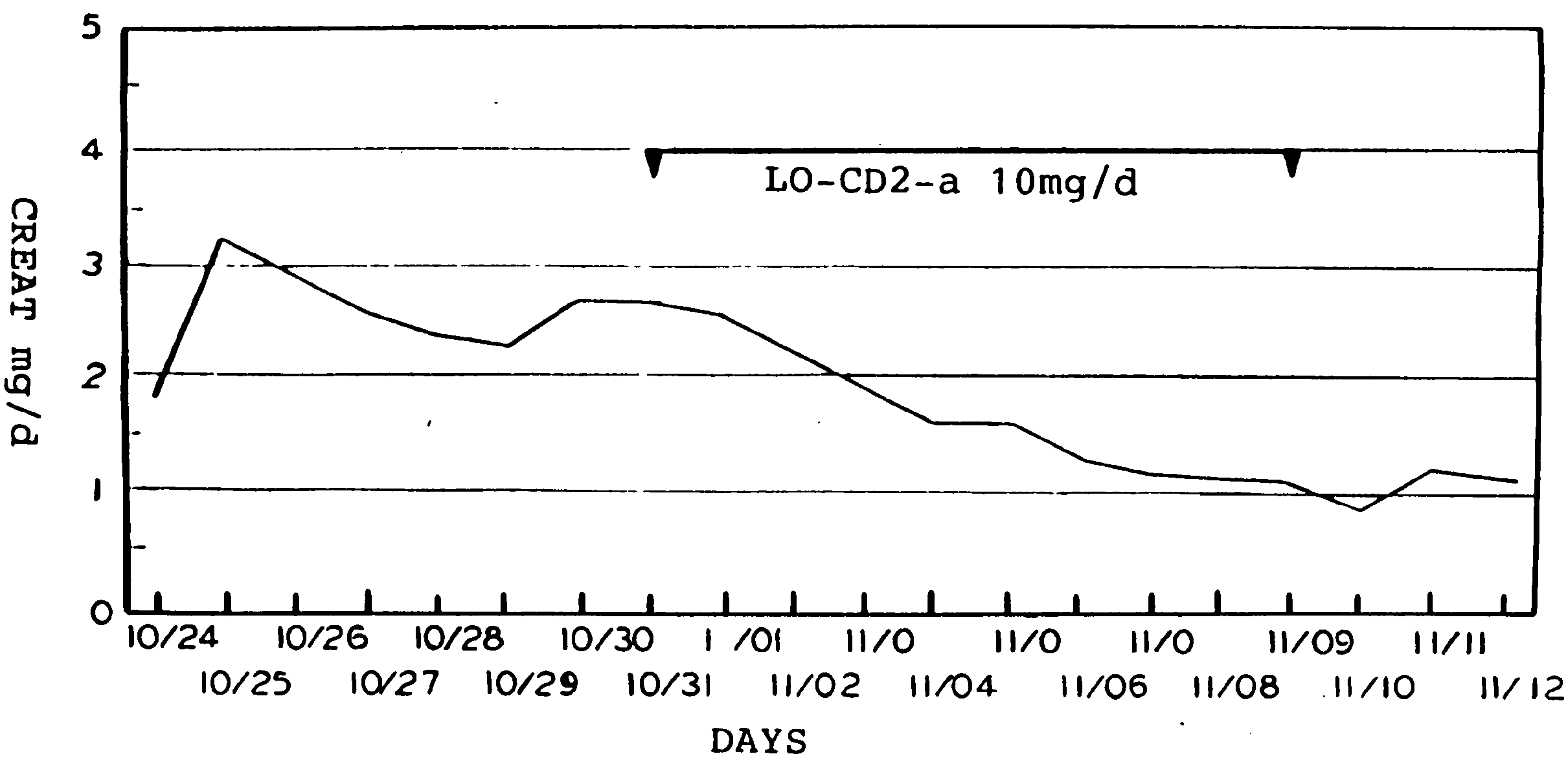


FIG. 21



B=BEFORE INJECTION
A=AFTER INJECTION

FIG. 22



LO-CD2-a 10mg/d
CREAT mg/d
5
4
3
2
1
0
10/24
10/25
10/26
10/27
10/28
10/29
10/30
10/31
1 /01
11/02
11/0
11/04
11/0
11/06
11/0
11/08
11/09
11/10
11/11
11/12
DAYS

CREAT

FIG. 23

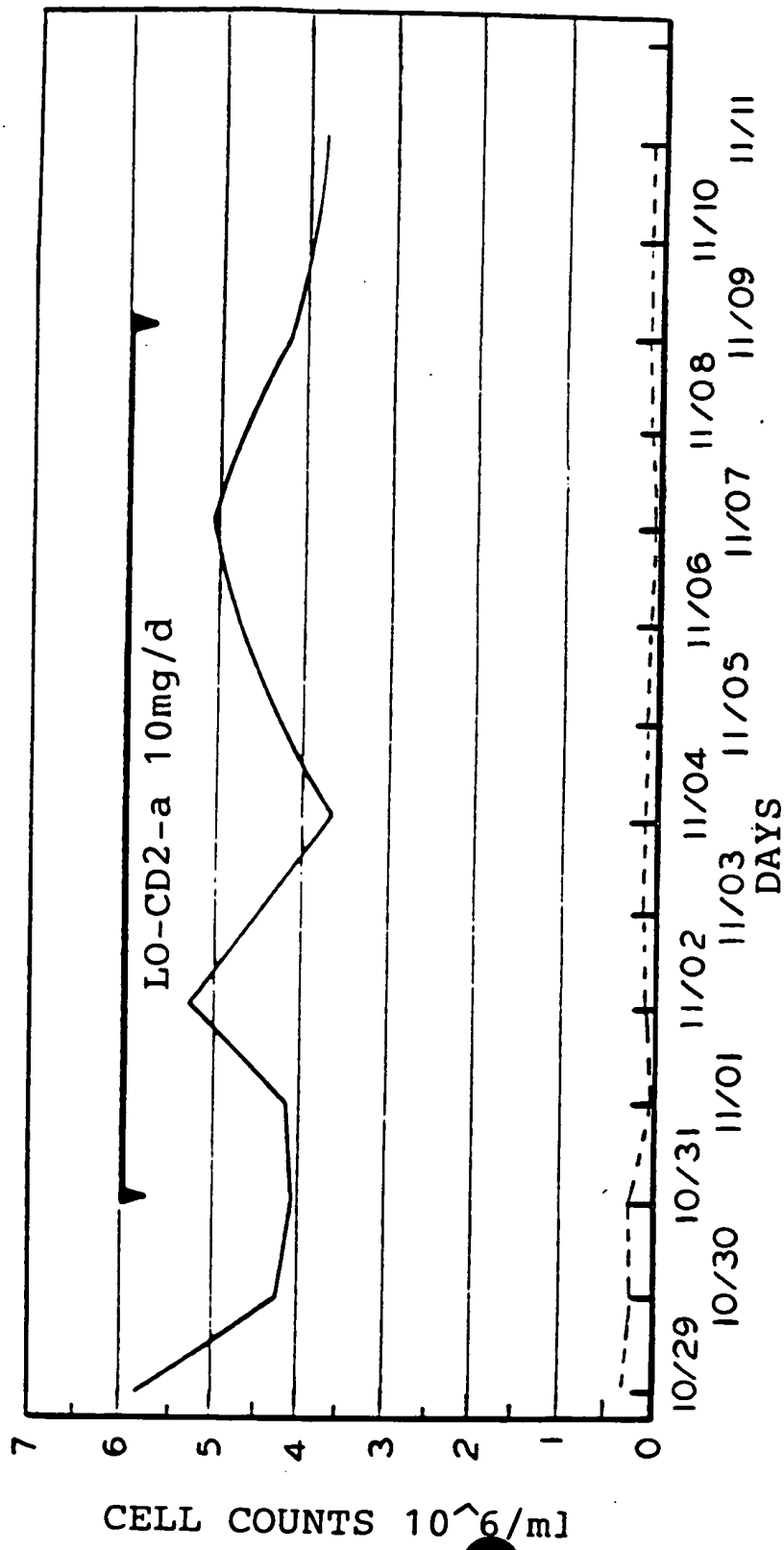
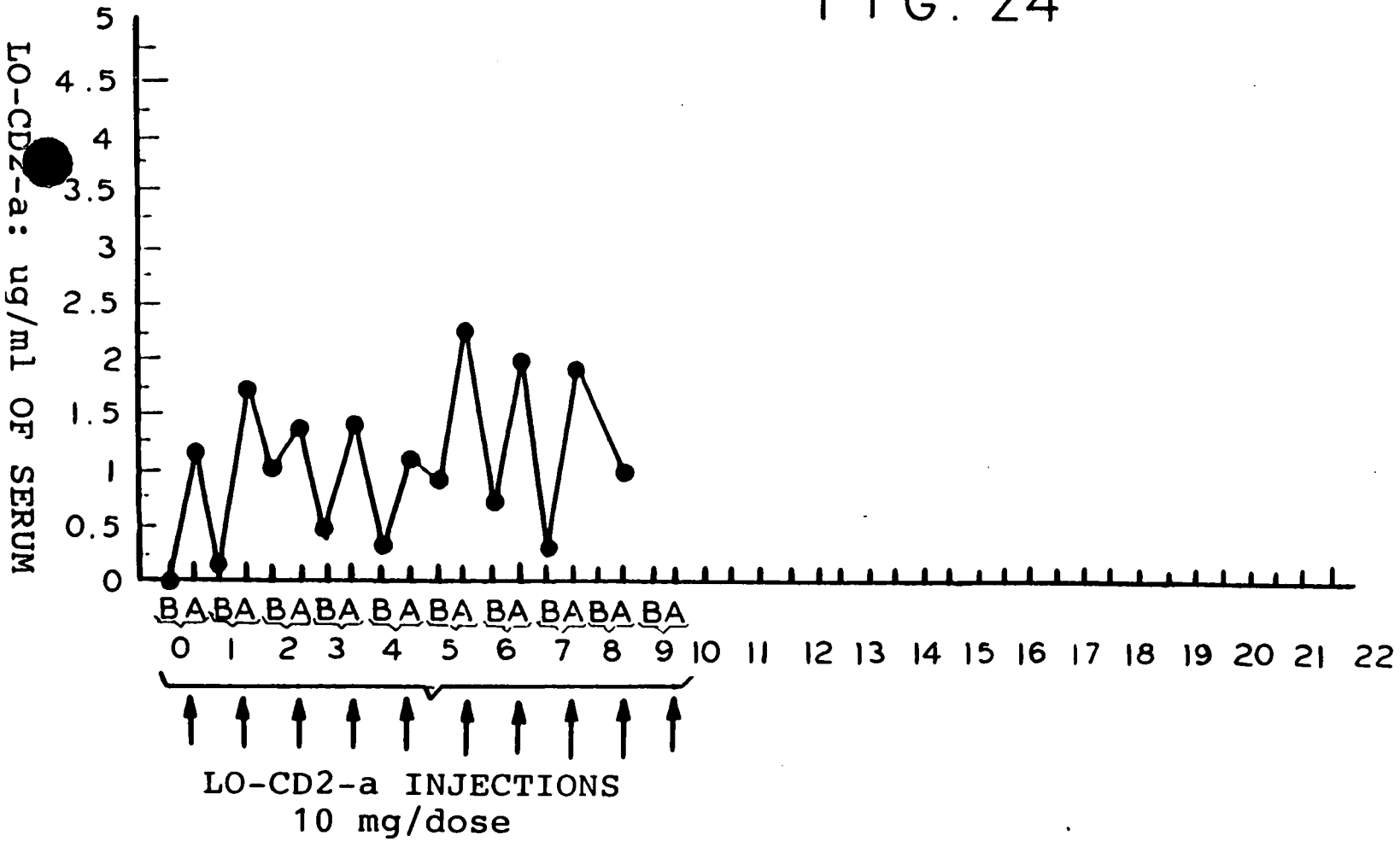
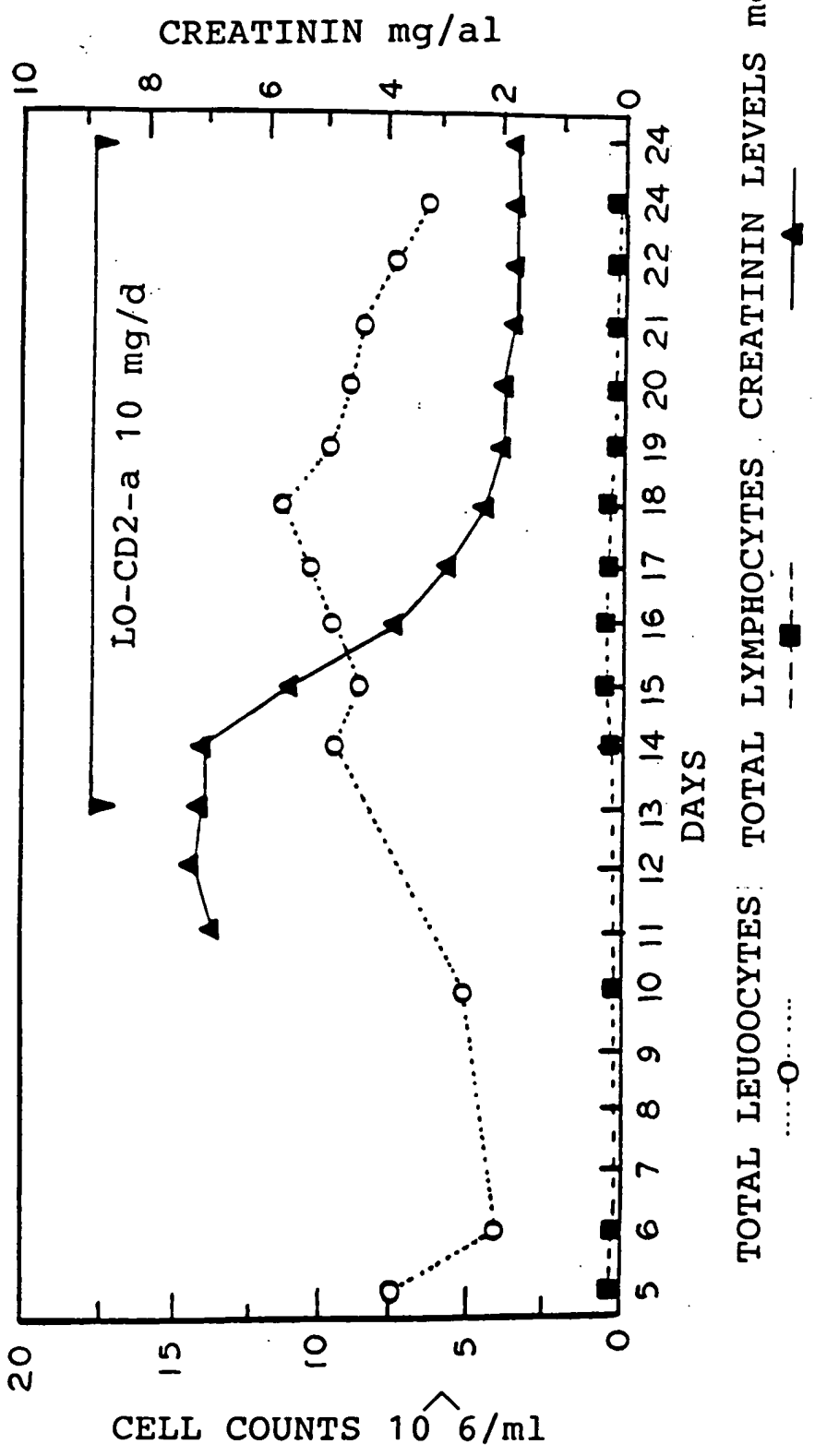

LO-CD2-a 10mg/d
CELL COUNTS 10^6/ml
0
1
2
3
4
5
6
7
10/29
10/30
10/31
11/01
11/02
11/03
11/04
11/05
11/06
11/07
11/08
11/09
11/10
11/11
DAYS
TOTLEUCO
LYC

FIG. 24



B=BEFORE INJECTIONS
A=25 HOURS AFTER INJECTIONS

FIG. 25



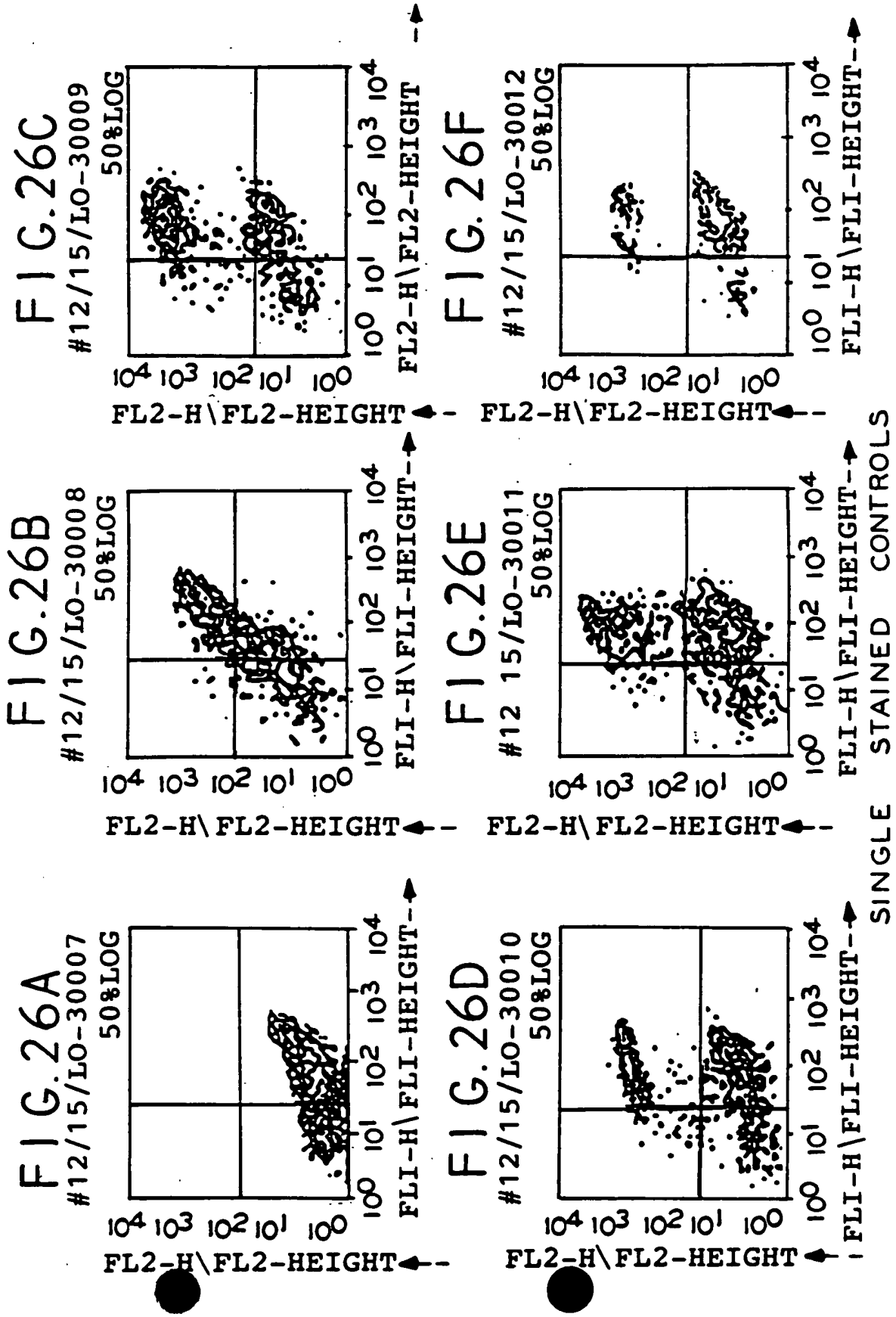


FIG.26C
#12/15/LO-30009
50%LOG
FL2-H\FL2-HEIGHT
FL2-H\FL2-HEIGHT
FIG.26F
#12/15/LO-30012
50%LOG
FL2-H\FL2-HEIGHT
FLI-H\FLI-HEIGHT
FIG.26B
#12/15/LO-30008
50%LOG
FL2-H\FL2-HEIGHT
FLI-H\FLI-HEIGHT
FIG.26E
#12 15/LO-30011
50%LOG
FL2-H\FL2-HEIGHT
FLI-H\FLI-HEIGHT
FIG.26A
#12/15/LO-30007
50%LOG
FL2-H\FL2-HEIGHT
FLI-H\FLI-HEIGHT
FIG.26D
#12/15/LO-30010
50%LOG
FL2-H\FL2-HEIGHT
FLI-H\FLI-HEIGHT
SINGLE STAINED CONTROLS

SINGLE STAINED CONTROLS

FIG. 26G

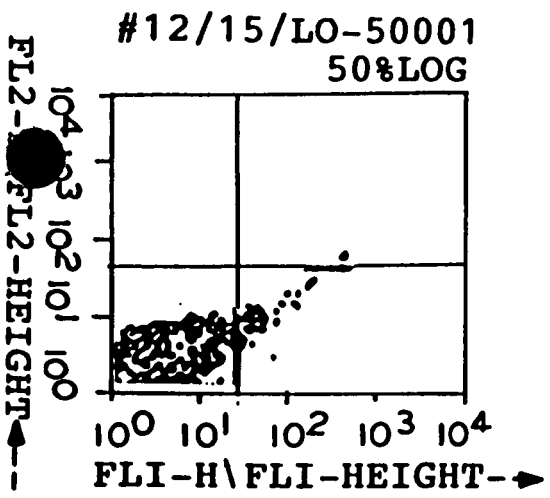


FIG. 26H

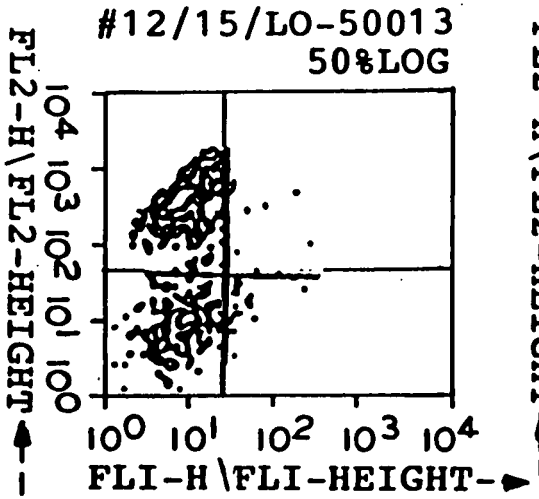


FIG. 26I

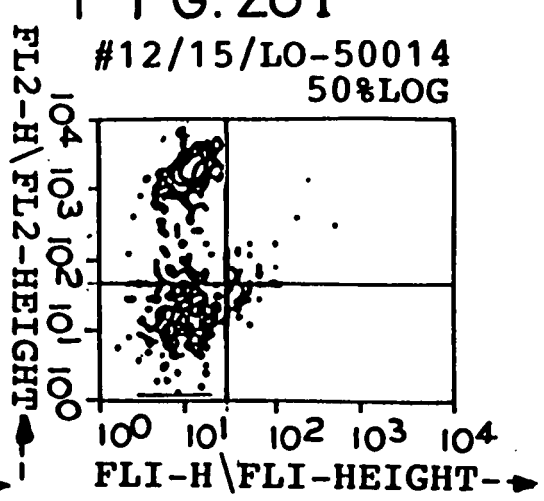


FIG. 26J

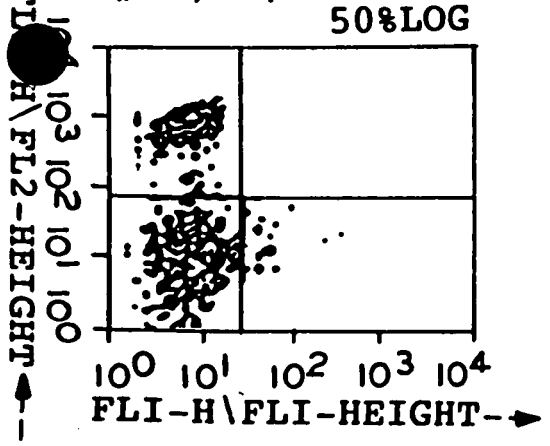


FIG. 26K

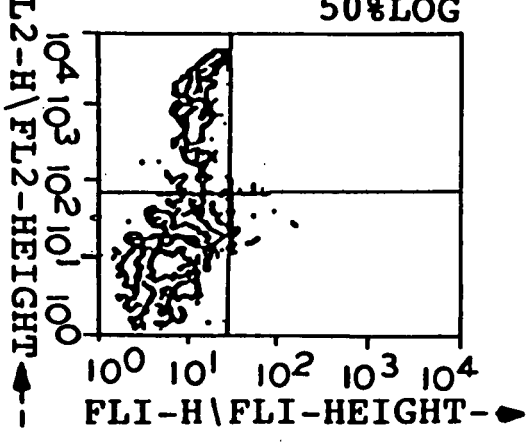


FIG. 26L

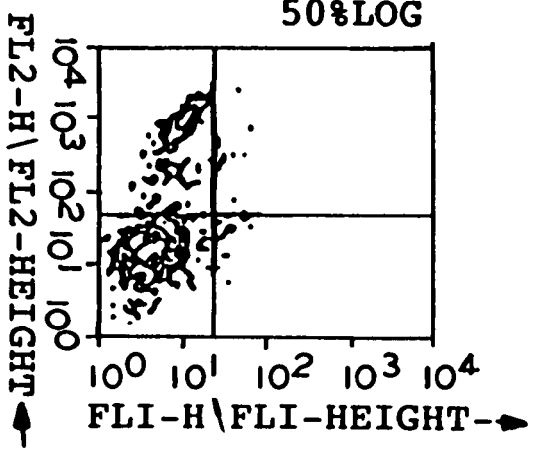


FIG. 27A

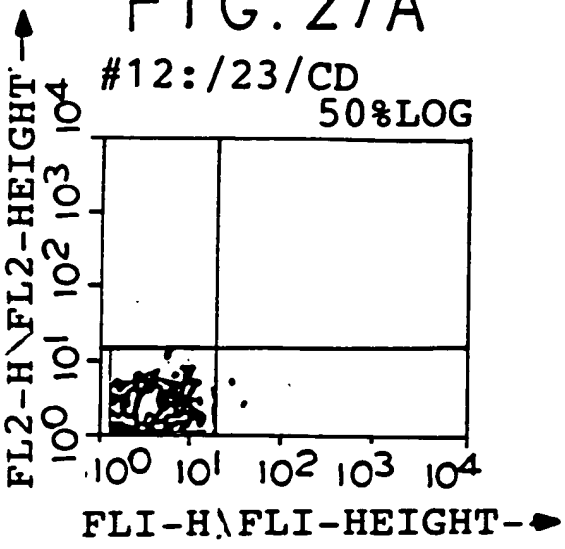


FIG. 27B

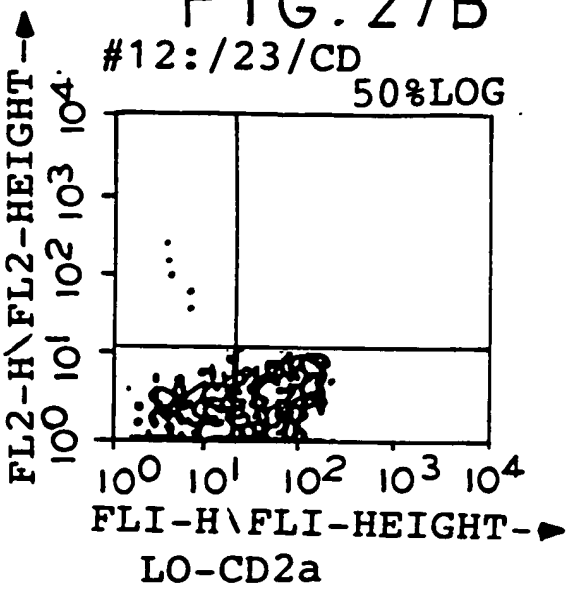


FIG. 27C

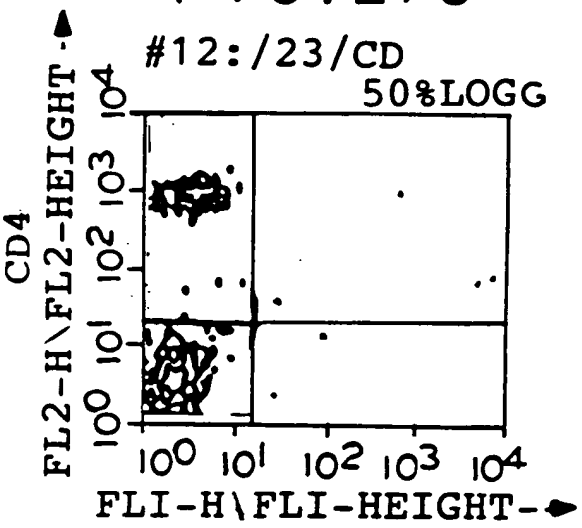


FIG. 27D

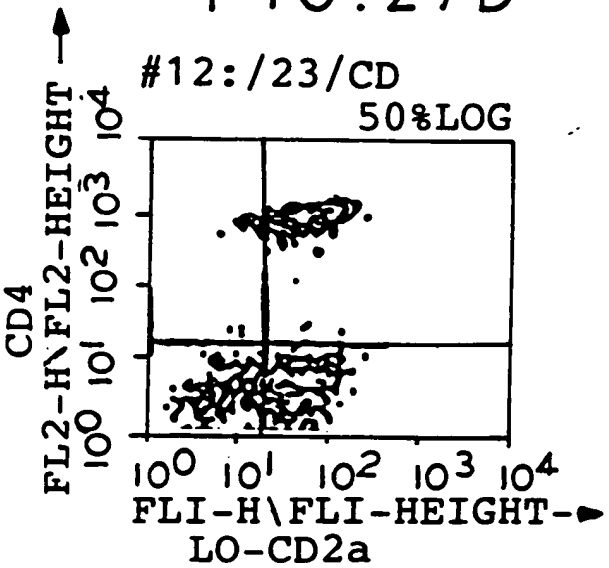


FIG. 27E

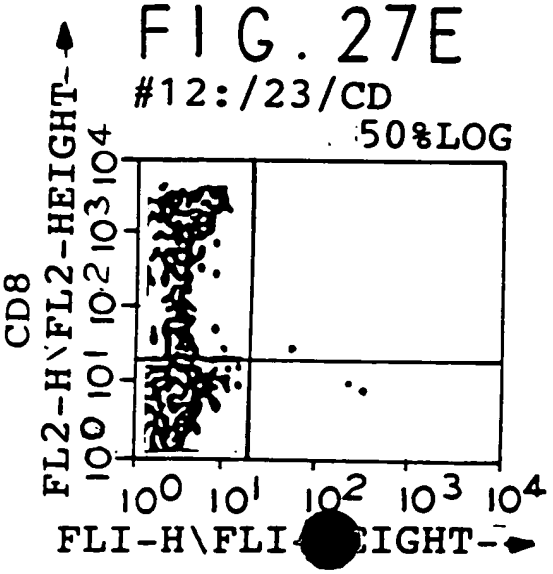


FIG. 27F

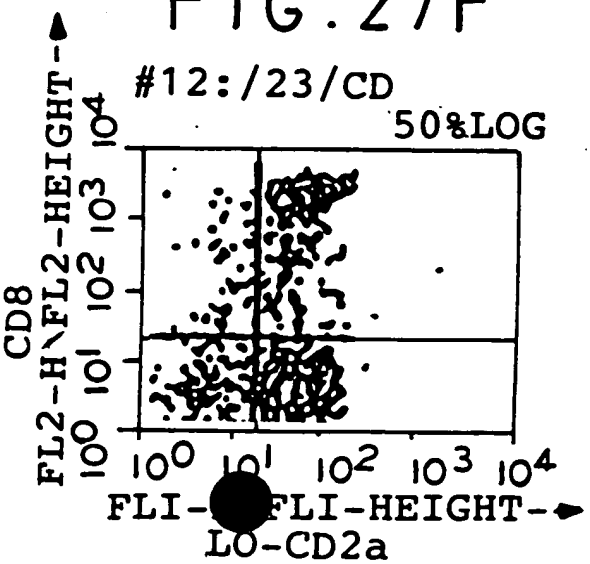


FIG.27G

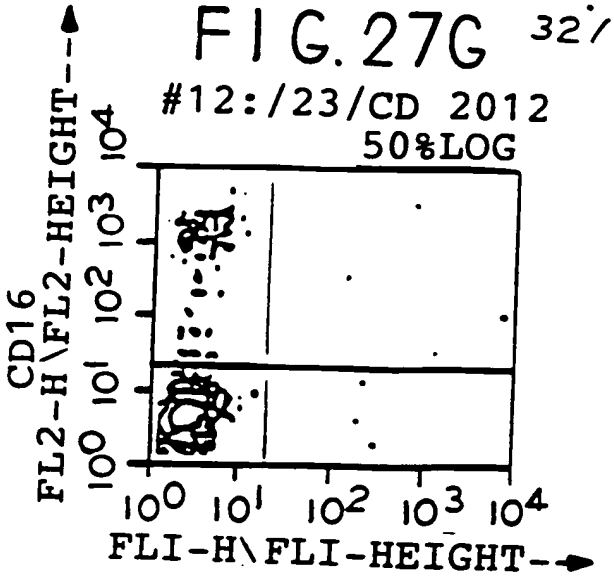


FIG.27H

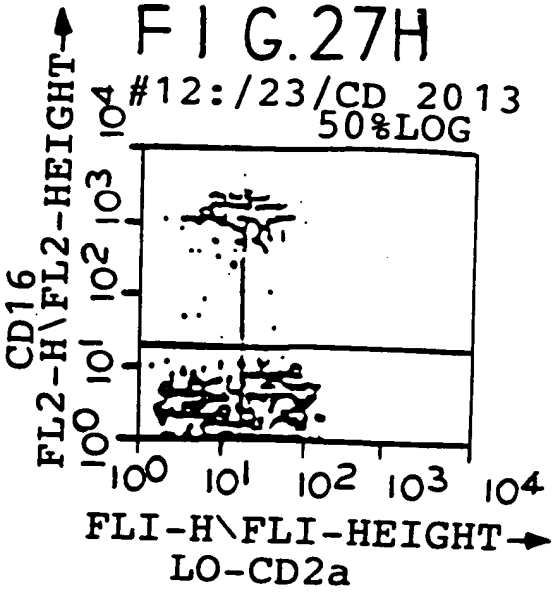


FIG.27I

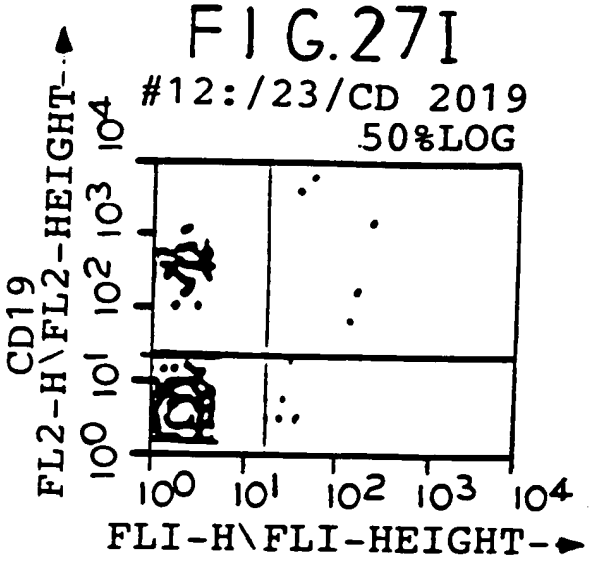


FIG.27J

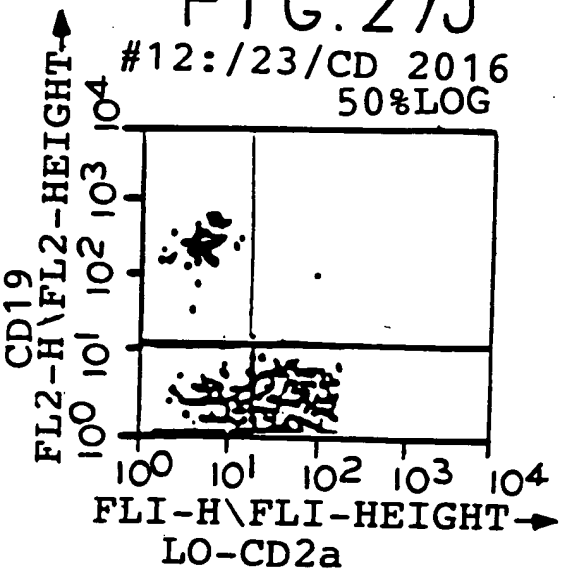


FIG.27K

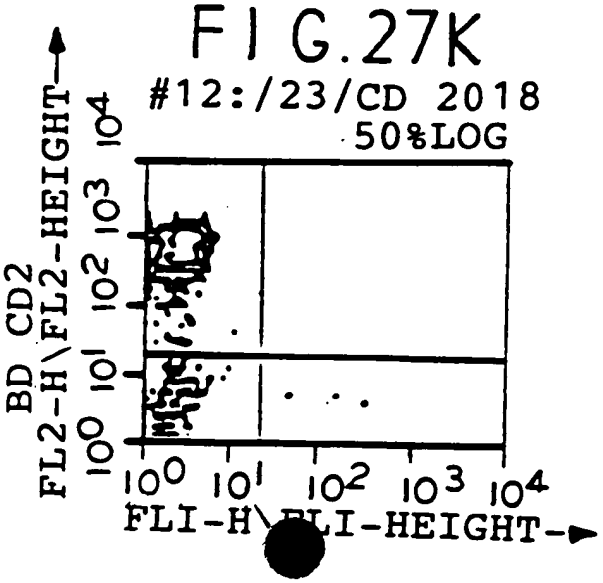


FIG.27L

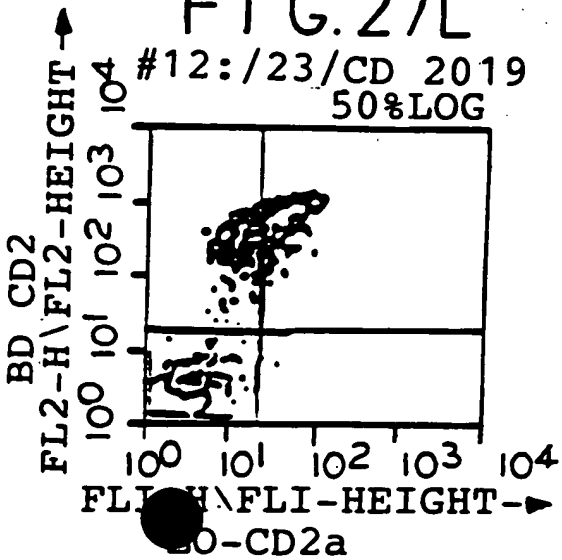


FIG.28A

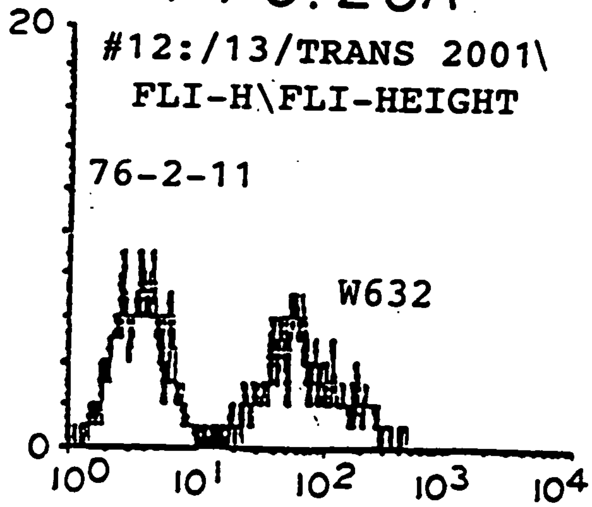


FIG.28B

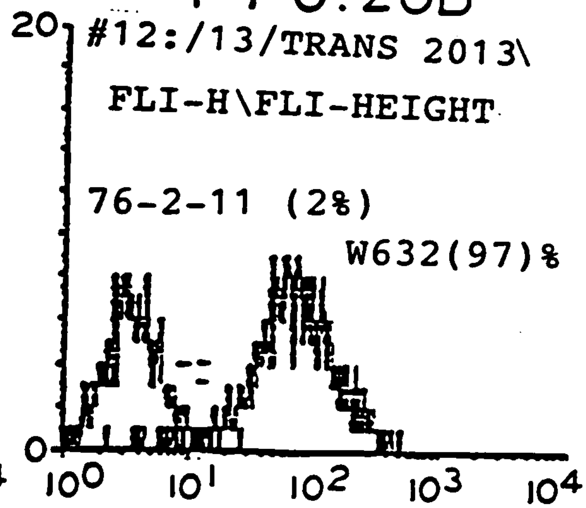


FIG.28C

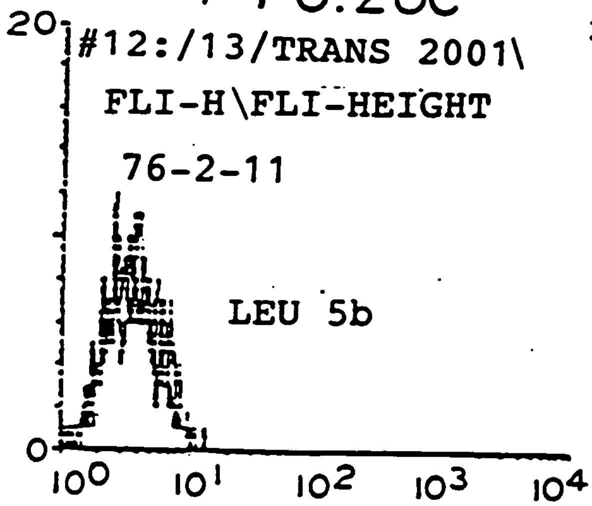


FIG.28D

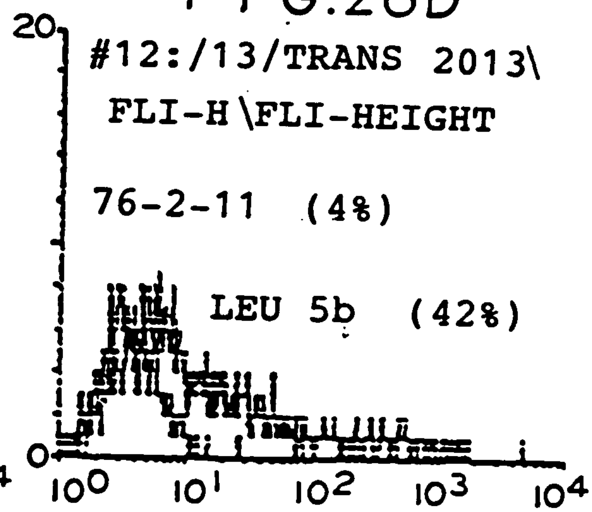


FIG.28E

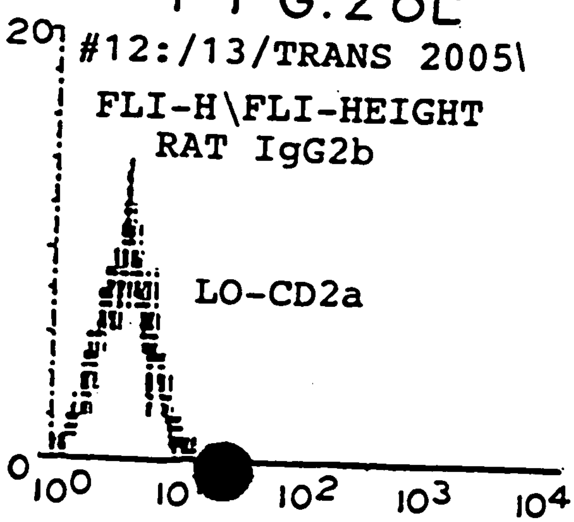


FIG.28F

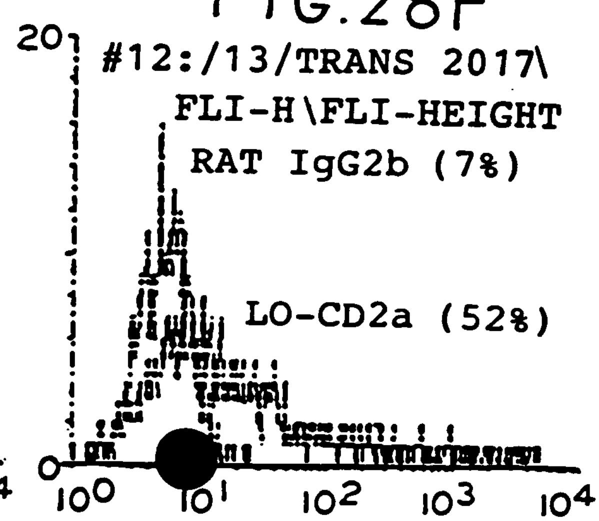
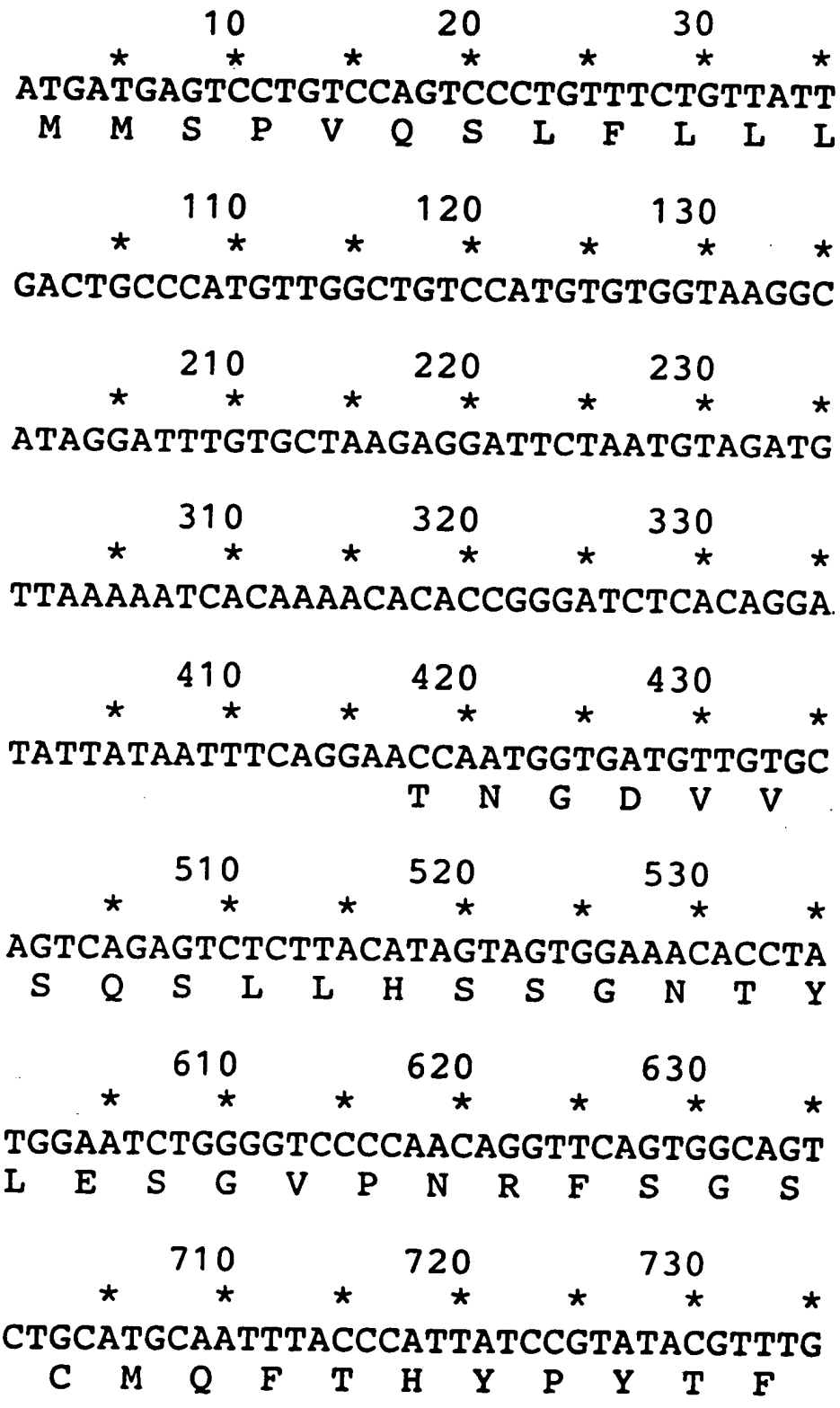
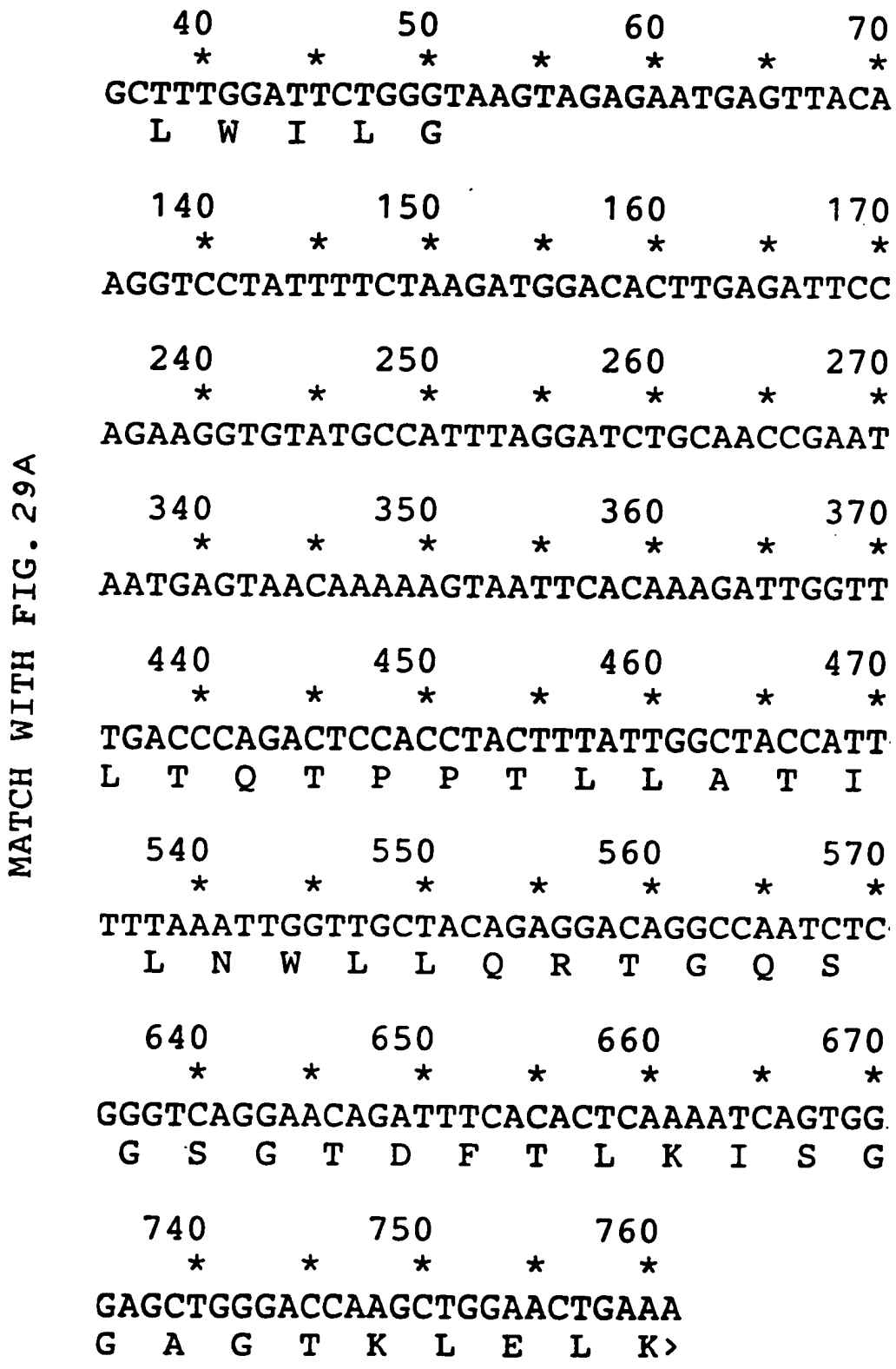


FIG. 29A



MATCH WITH FIG. 29B

FIG.29B



MATCH WITH FIG. 29A

MATCH WITH FIG. 29C

FIG. 29C

MATCH WITH FIG. 29B

```
        80          90          100
    *   *   *   *   *   *
GGACAAGAATGGGGATGGAGGATGAGTTCT

       180         190         200
    *   *   *   *   *   *
ATTACTTGATAATGAGAAATTACAGATGAG

       280         290         300
    *   *   *   *   *   *
TGTTTTGTGAAAAAGCATTTGGTATATTTT

       380         390         400
    *   *   *   *   *   *
GCAAATTTTGCACATAACTTTGTTCTGATC

       480         490         500
    *   *   *   *   *   *
GGACAATCAGTCTCCATCTCTTGCAGGTCA
 G   Q   S   V   S   I   S   C   R   S>

       580         590         600
    *   *   *   *   *   *
CACAGCCGCTAATTTATTTGGTATCCAAAC
P   Q   P   L   I   Y   L   V   S   K>

       680         690         700
    *   *   *   *   *   *
AGTGGAAGTTGAGGATTTGGGGGTTTATTA
  V   E   A   E   D   L   G   V   Y   Y>
```

FIG. 30A

```
        10         20         30         40
    *    *    *    *    *    *    *    *    *
ATGAAATGCAGGTGGATCATCTTCTTCTTGATGGCAGTAGCTACAG
 M  K  C  R  W  I  I  L  F  L  M  A  V  A  T

       110        120        130        140
    *    *    *    *    *    *    *    *    *
CACTATCTTTGGATTTCTTGCAACAGGGGTCAACTCAGAAGTTCAG
                                 V  N  S  E  V  Q

       210        220        230        240
    *    *    *    *    *    *    *    *    *
TGCAAGGCTTCTGGCTATATATTTATAGAATACTATATGTACTGGG
 C  K  A  S  G  Y  I  F  T  E  Y  Y  M  Y  W

       310        320        330        340
    *    *    *    *    *    *    *    *    *
ACGGTAGTATTGATTATGTTGAGAAGTTCAAAAAGAAGGCCACACT
D  G  S  I  D  Y  V  E  K  F  K  K  K  A  T  L

       410        420        430        440
    *    *    *    *    *    *    *    *    *
TGAGGACACAGCAACCTATTTTTGTGCTAGGGGAAAATTCAACTAT
  E  D  T  A  T  Y  F  C  A  R  G  K  F  N  Y
```

Match with FIG. 30B

FIG. 30B

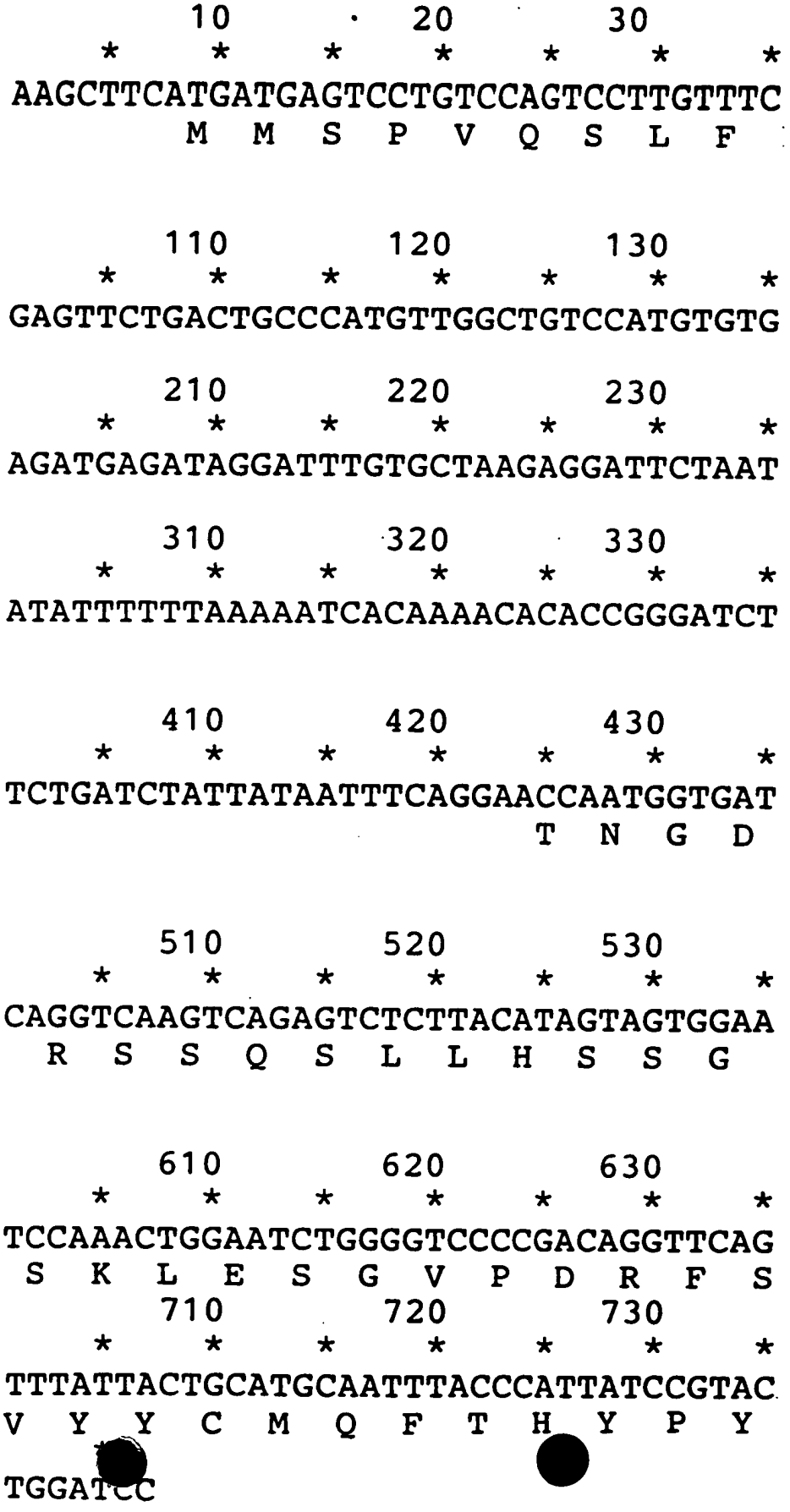
```
50        60        70        80        90        100
 *    *    *    *    *    *    *    *    *    *    *
GTAAGGCACTCCCAAGTCCTAAACTTGAGAGATCATACACTTGG GAGACAGTGA
G>

150       160       170       180       190       200
 *    *    *    *    *    *    *    *    *    *    *
CTGCAGCAATCTGGGCCTGAGCTTCAGAGACCCGGGGCCTCAGT CAAGTTGTCG
 L  Q  Q  S  G  P  E  L  Q  R  P  G  A  S  V  K  L  S>

250       260       270       280       290       300
 *    *    *    *    *    *    *    *    *    *    *
TGAAGCAGAGGCCTAAACAGGGCCTGGAATTAGTAGGAAGGATC GATCCTGAAG
V  K  Q  R  P  K  Q  G  L  E  L  V  G  R  I  D  P  E>

350       360       370       380       390       400
 *    *    *    *    *    *    *    *    *    *    *
GACTGCAGATACATCGTCCAATACAGCCTACATGCAACTTAGCA GCCTGACATC
  T  A  D  T  S  S  N  T  A  Y  M  Q  L  S  S  L  T  S>

450       460       470       480       490
 *    *    *    *    *    *    *    *    *
CGATTTGCTTACTGGGGCCAAGGCACCCTCGTCACAGTCTCCTC A
 R  F  A  Y  W  G  Q  G  T  L  V  T  V  S  S>
```

MATCH WITH FIG. 30A

FIG. 31

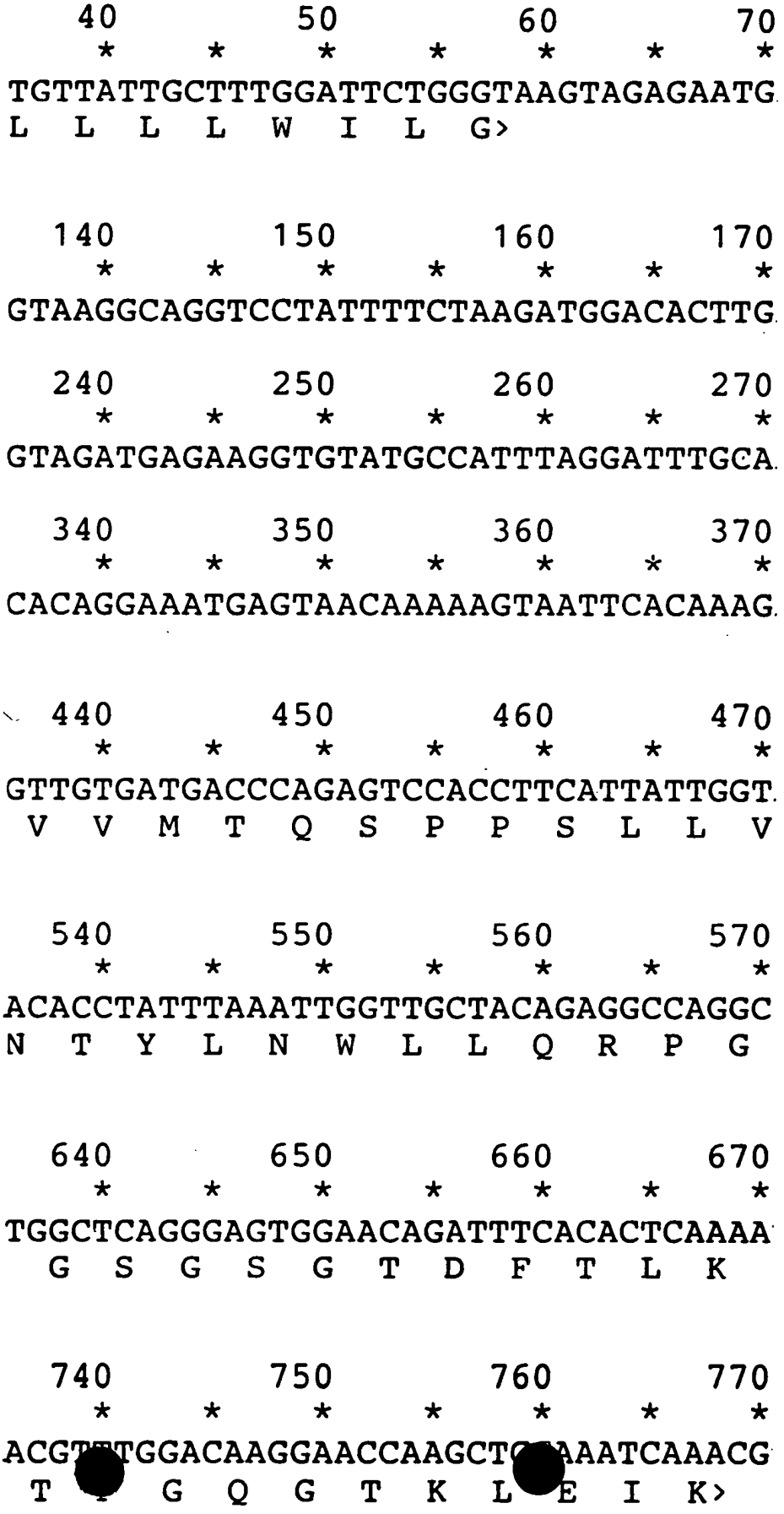
```
                   FR 1                       CDR 1
                      *   *         20         30                40 **   FR 2
                                                                              *
Rat Lo-CD2a Vk     DVVLTQTPPT LLATIGQSVS ISCRSSQSLL HSSGNTYLNW LLQRTGQSPQ
Humanized Vk       ---M--S--S --V-L--PA- ---------- ---------- ----P-----
Human HUM5400 Vk   ---M--S-LS -PV-L--PA-  -        -V Y-D---H--- FQ--P----R

                    CDR 2                 FR 3
                     60        70         80         90         CDR 3
                   *                                 *                100
Rat LO-CD2a Vk     PLIYLVSKLE SGVPNRFSGS GSGTDFTLKI SGVEAEDLGV YYCMQFTHYP
Humanized Vk       ---------- ----D----- ---------- -------V-- ----------
HumanHUM5400 Vk    R---K--NRD ----D----- ---------- -R-----V-- -----G--W-

                      FR 4
                      110
Rat LO-CD2a Vk     YTFGAGTKLE LK
Humanized Vk       ----Q----- I-
HumanHUM5400 Vk    ----Q----- I-
```

FIG. 32A



MATCH WITH FIG. 32B

FIG. 32B



MATCH WITH FIG. 32A

MATCH WITH FIG. 32C

FIG. 32C

```
          80          90          100
     *    *    *    *    *    *
AGTTACAGGACAAGAATGGGGATGGAGGAT

          180         190         200
     *    *    *    *    *    *
AGATTCCATTACTTGATAATGAGAAATTAC

          280         290         300
     *    *    *    *    *    *
ACCAATTGTTTGTTGAAAAAAGCATTTGGT

          380         390         400
     *    *    *    *    *    *
ATTGGTTGCAAATTTTGCACATAACTTTGT

          480         490         500
     *    *    *    *    *    *
AACCTTGGGACAACCAGCTTCCATCTCTTG
  T   L   G   Q   P   A   S   I   S   C>

          580         590         600
     *    *    *    *    *    *
CAATCTCCACAGCCGCTAATTTATTTGGTA
 Q   S   P   Q   P   L   I   Y   L   V>

          680         690         700
     *    *    *    *    *    *
TCAGTGGAGTGGAAGCTGAGGATGTGGGGG
I   S   G   V   E   A   E   D   V   G>

          780         790         800
     *    *    *    *    *    *
TGAGTAGAATTTAAACTT[redacted]CTTCCTCAGT
```

MATCH WITH FIG. 32B

FIG. 33

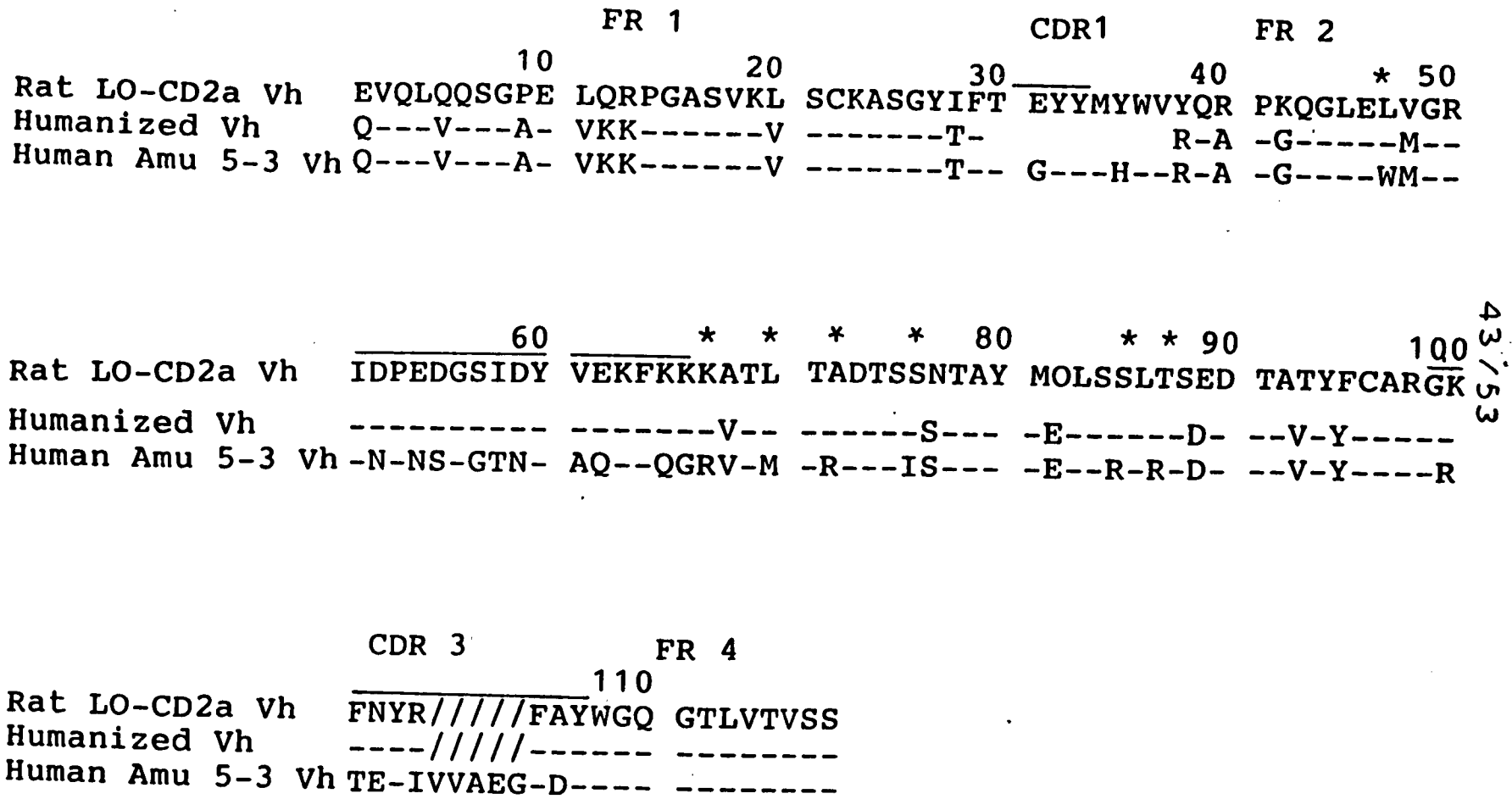
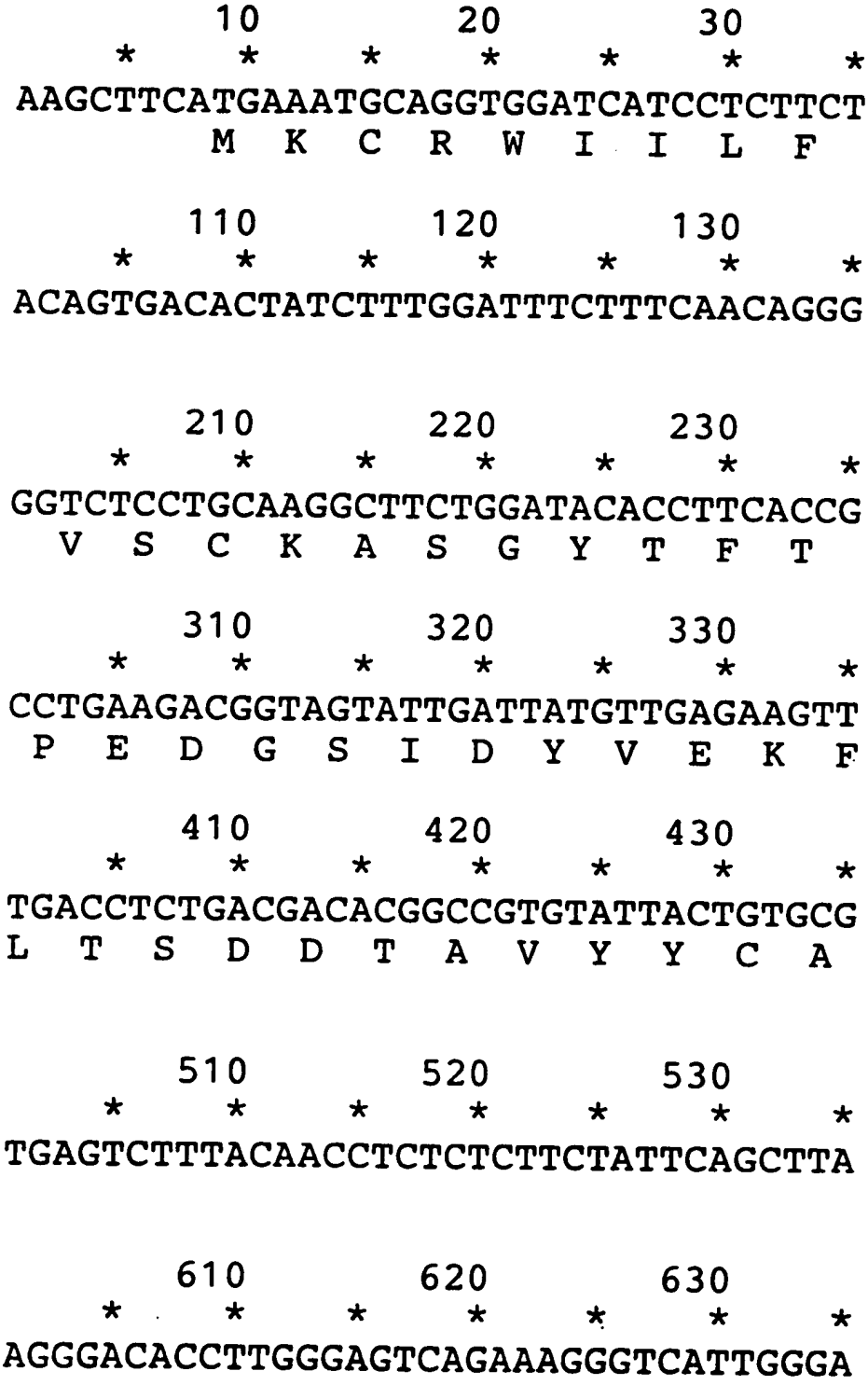
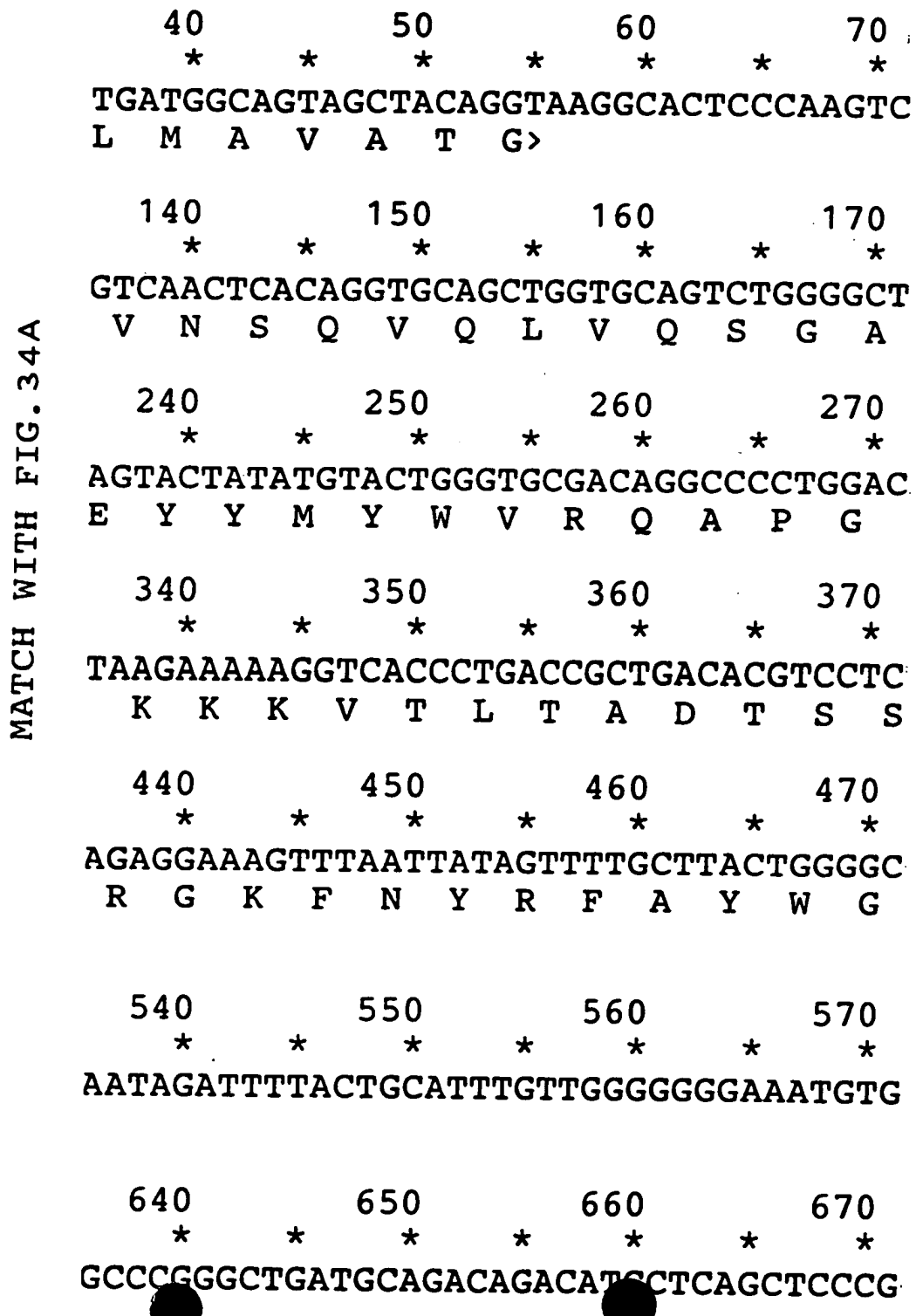

FR 1
CDR1
FR 2
10
20
30
40
50
Rat LO-CD2a Vh EVQLQQSGPE LQRPGASVKL SCKASGYIFT EYYMYWVYQR PKQGLELVGR
Humanized Vh Q---V---A- VKK-------V --------T- R-A -G-----M--
Human Amu 5-3 Vh Q---V---A- VKK-------V --------T-- G---H--R-A -G----WM--
60
80
90
100
Rat LO-CD2a Vh IDPEDGSIDY VEKFKKKATL TADTSSNTAY MQLSSLTSED TATYFCARGK
Humanized Vh ---------- --------V-- ------S--- -E------D- --V-Y-----
Human Amu 5-3 Vh -N-NS-GTN- AQ--QGRV-M -R---IS--- -E--R-R-D- --V-Y----R
CDR 3
FR 4
110
Rat LO-CD2a Vh FNYR/////FAYWGQ GTLVTVSS
Humanized Vh ----/////------ --------
Human Amu 5-3 Vh TE-IVVAEG-D---- --------

FIG. 34A



MATCH WITH FIG. 34B

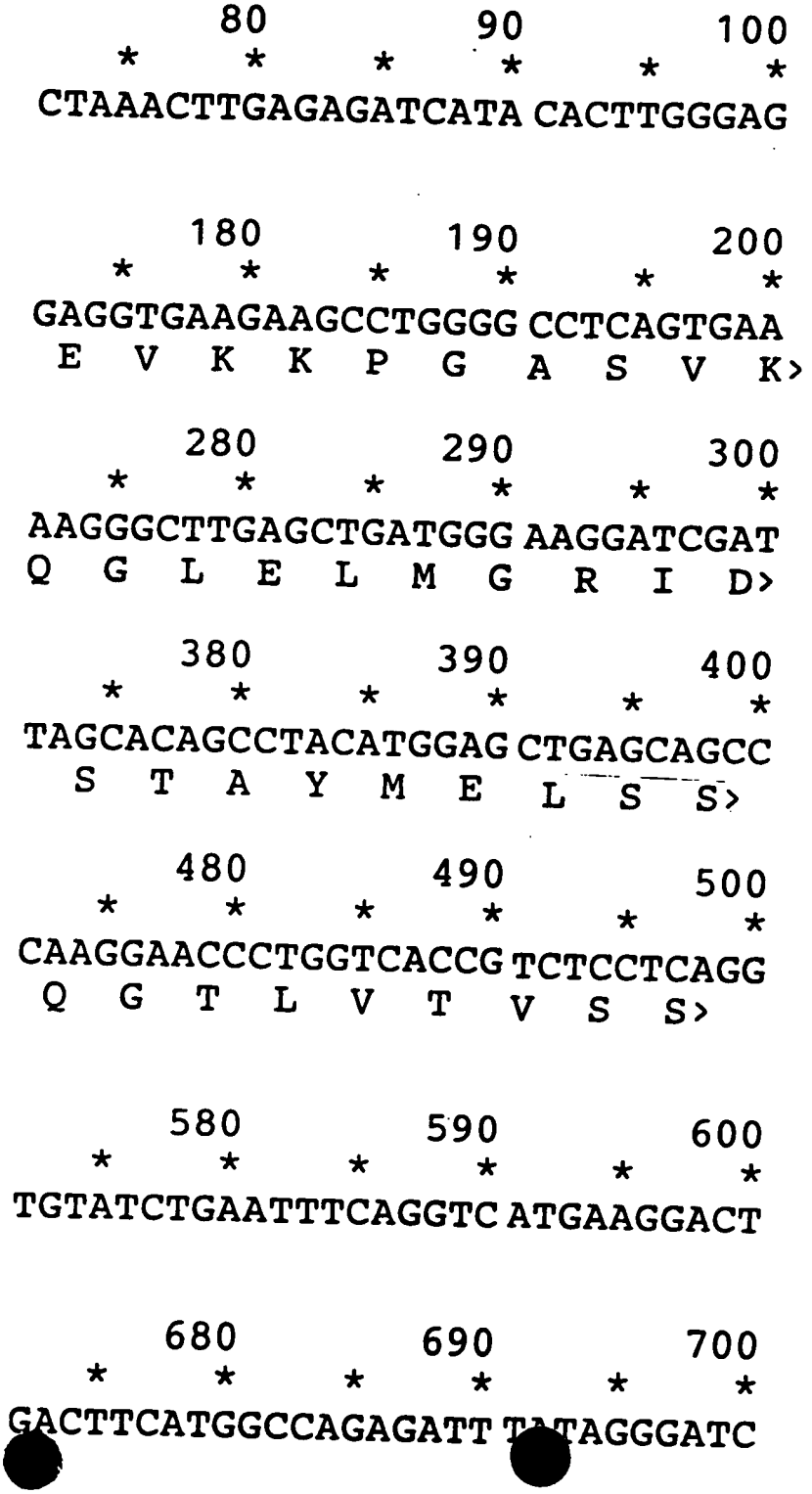
FIG. 34B



MATCH WITH FIG. 34A

MATCH WITH FIG. 34C

FIG. 34C



MATCH WITH FIG. 34B

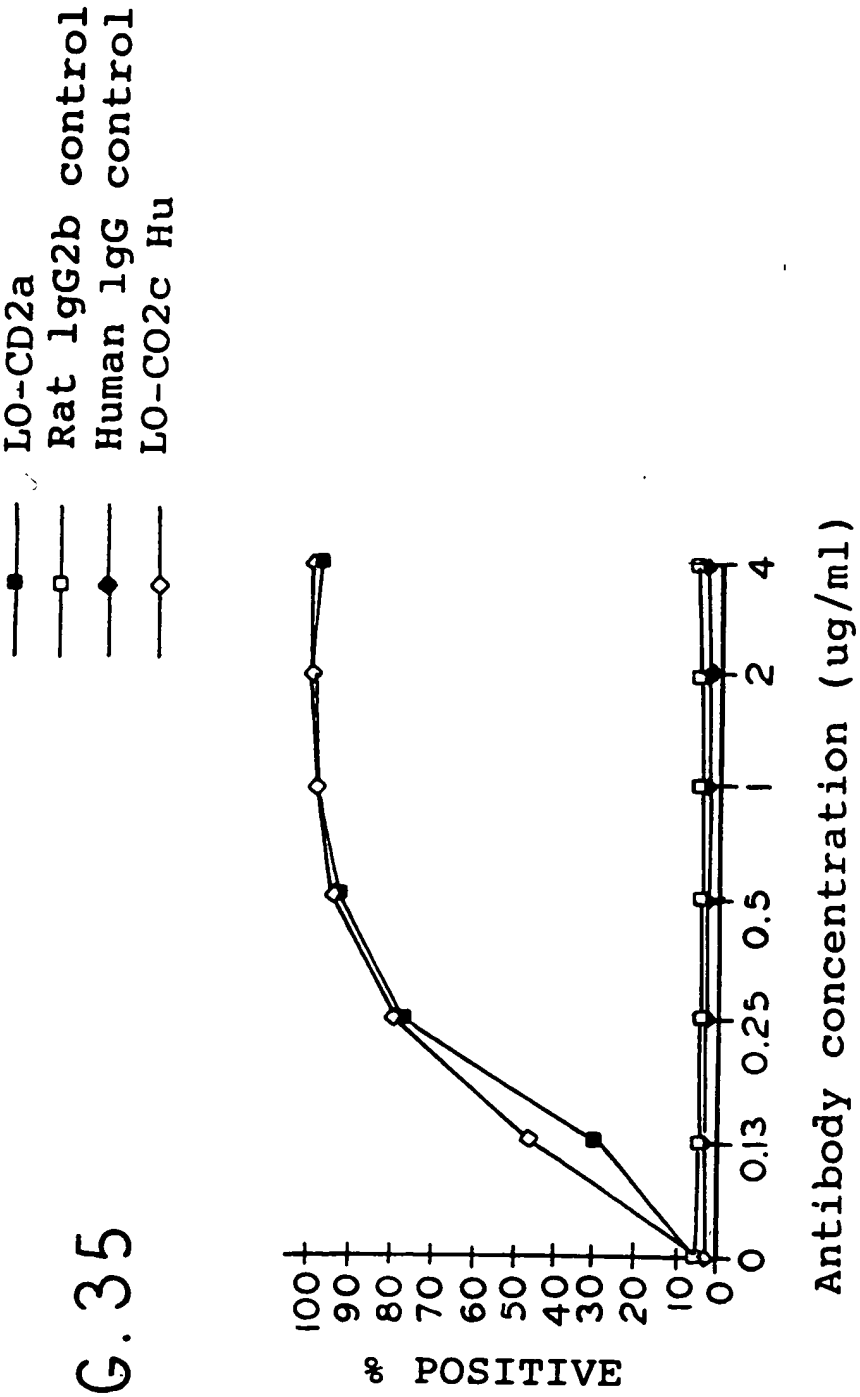


FIG. 35

FIG. 36

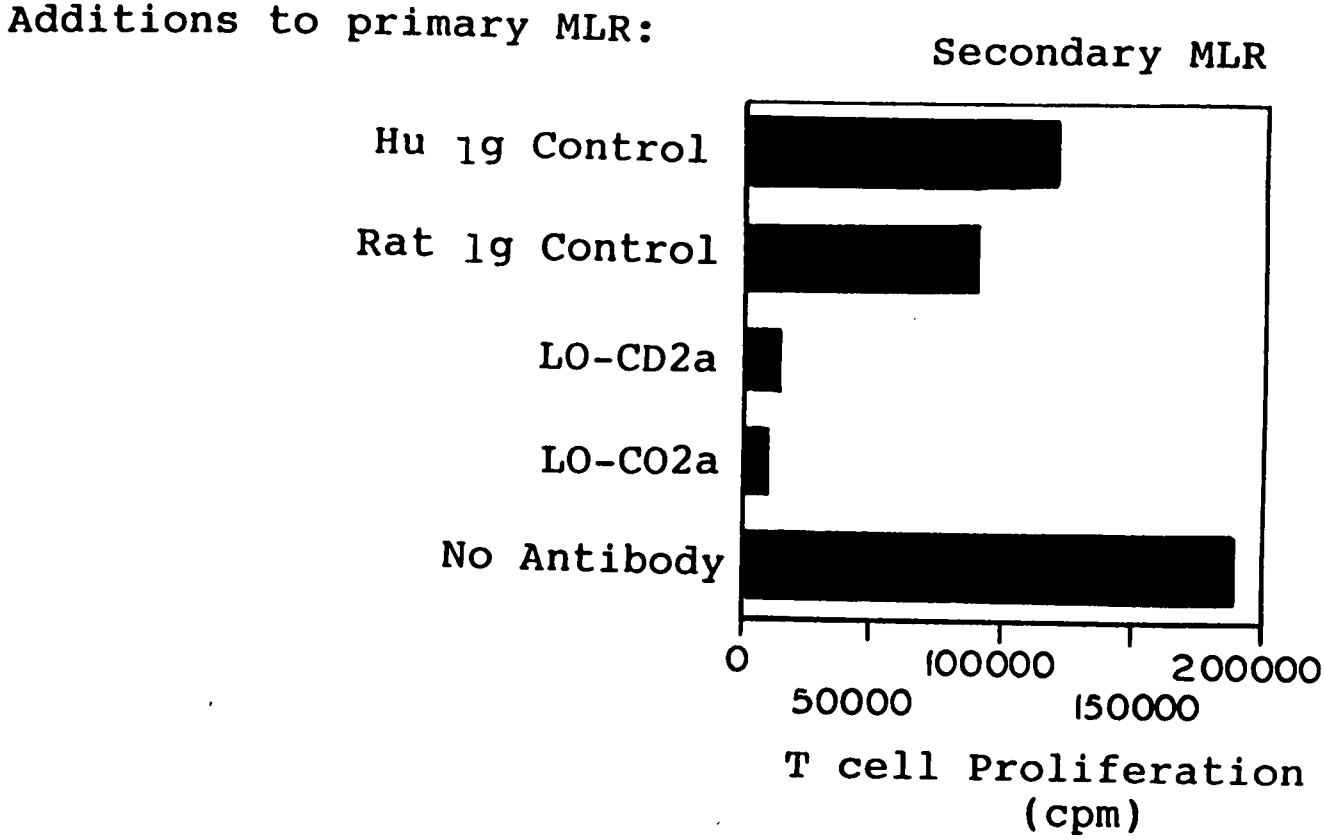

Additions to primary MLR:
Secondary MLR
Hu 1g Control
Rat 1g Control
LO-CD2a
LO-CO2a
No Antibody
0
50000
100000
150000
200000
T cell Proliferation
(cpm)

FIG. 37

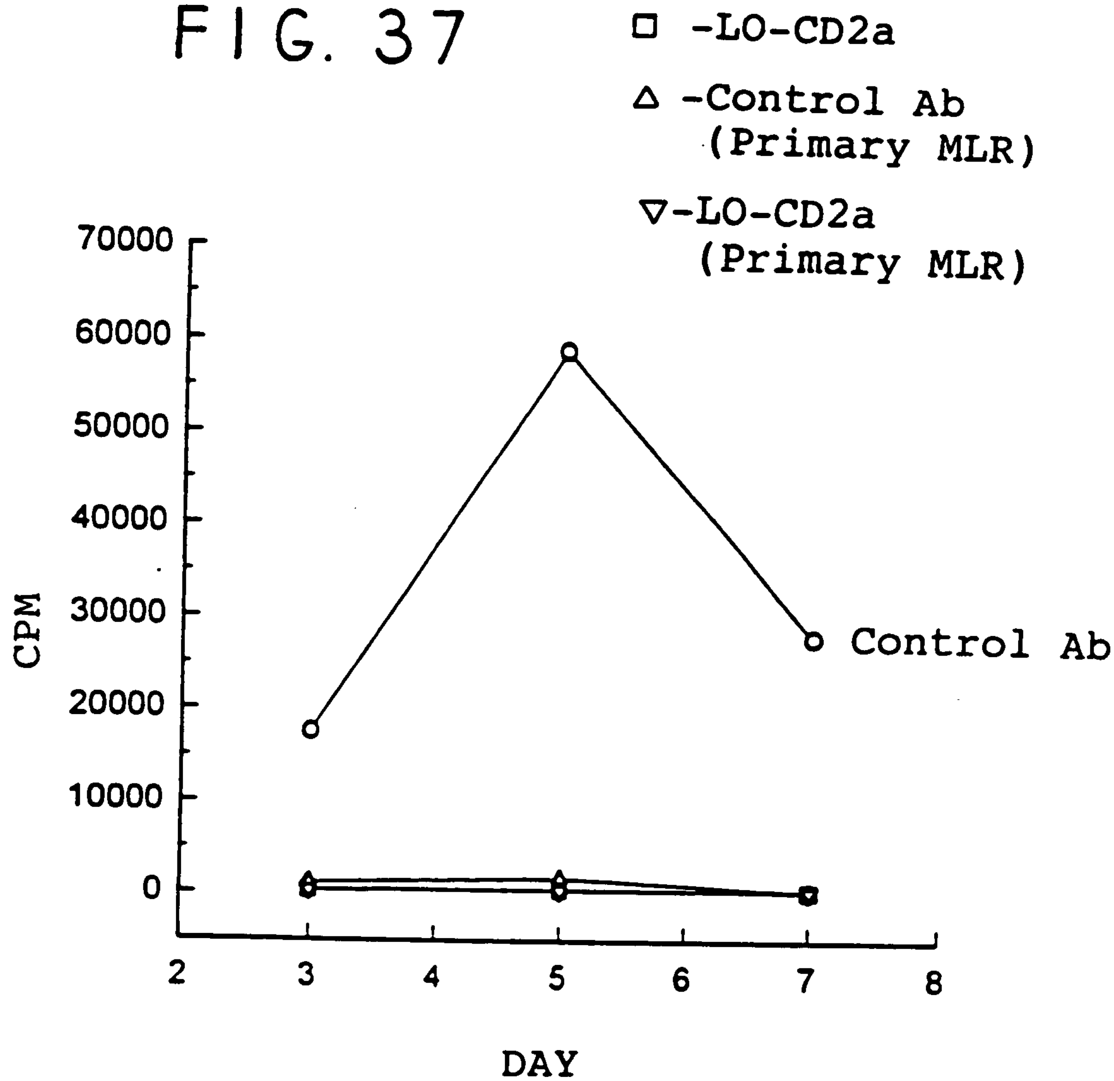


FIG. 38A

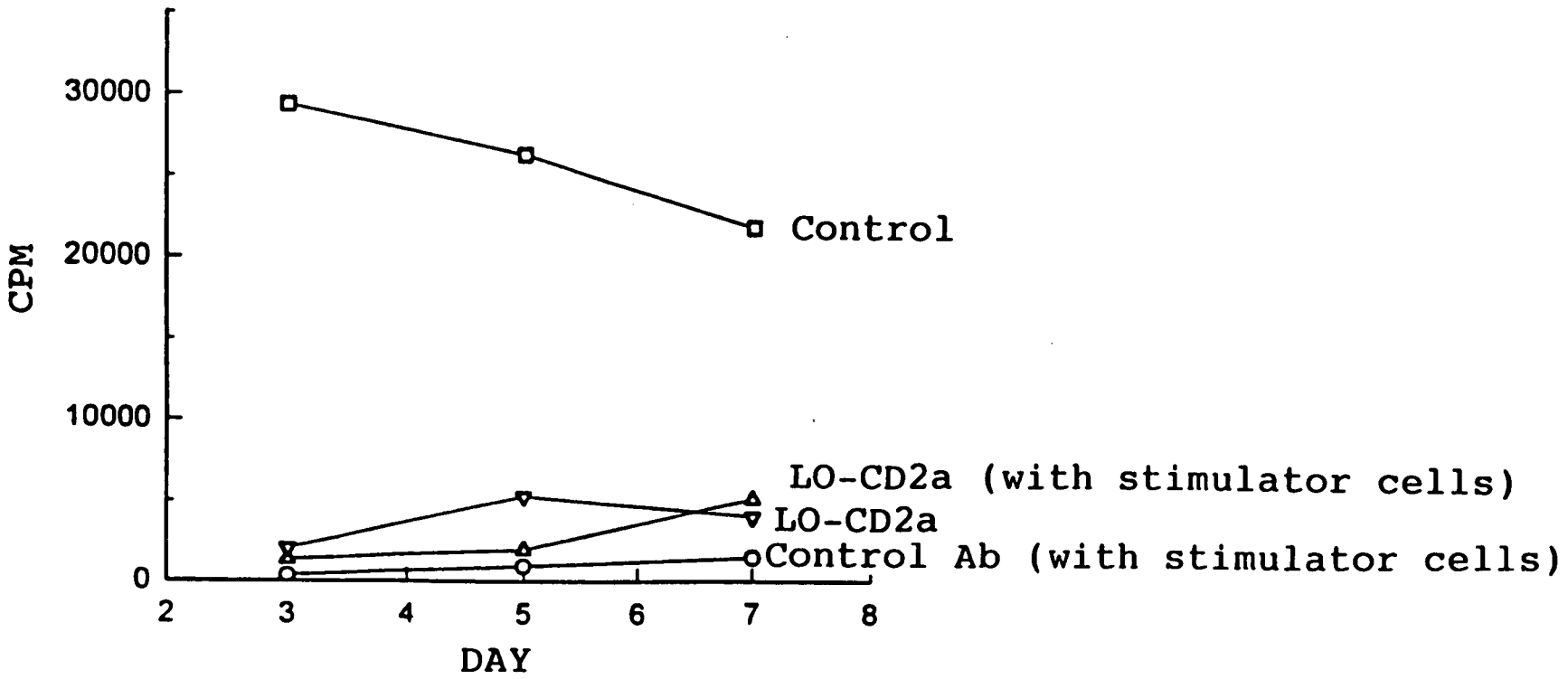

30000
20000
10000
0
CPM
2
3
4
5
6
7
8
DAY
Control
LO-CD2a (with stimulator cells)
LO-CD2a
Control Ab (with stimulator cells)

FIG. 38B

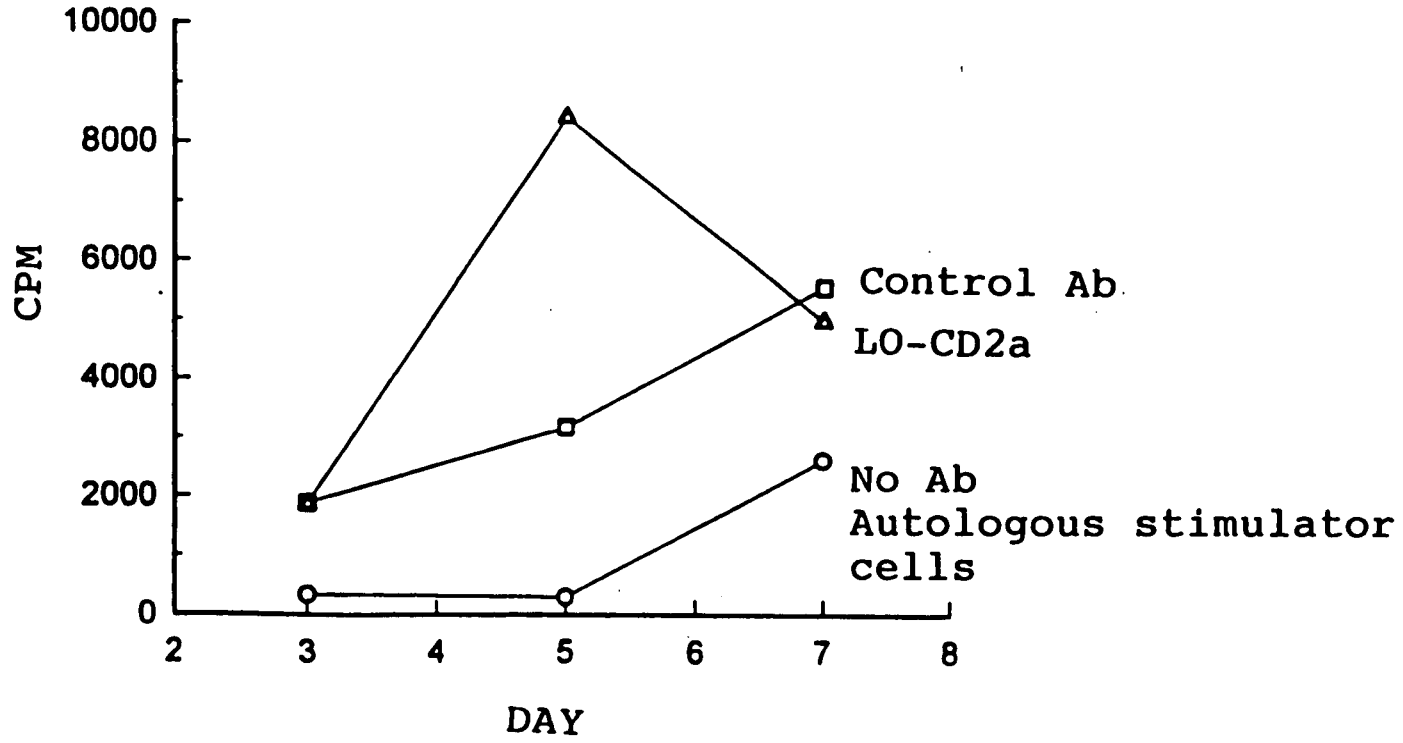

10000
8000
6000
4000
2000
0
CPM
2
3
4
5
6
7
8
DAY
Control Ab
LO-CD2a
No Ab
Autologous stimulator cells

FIG. 39

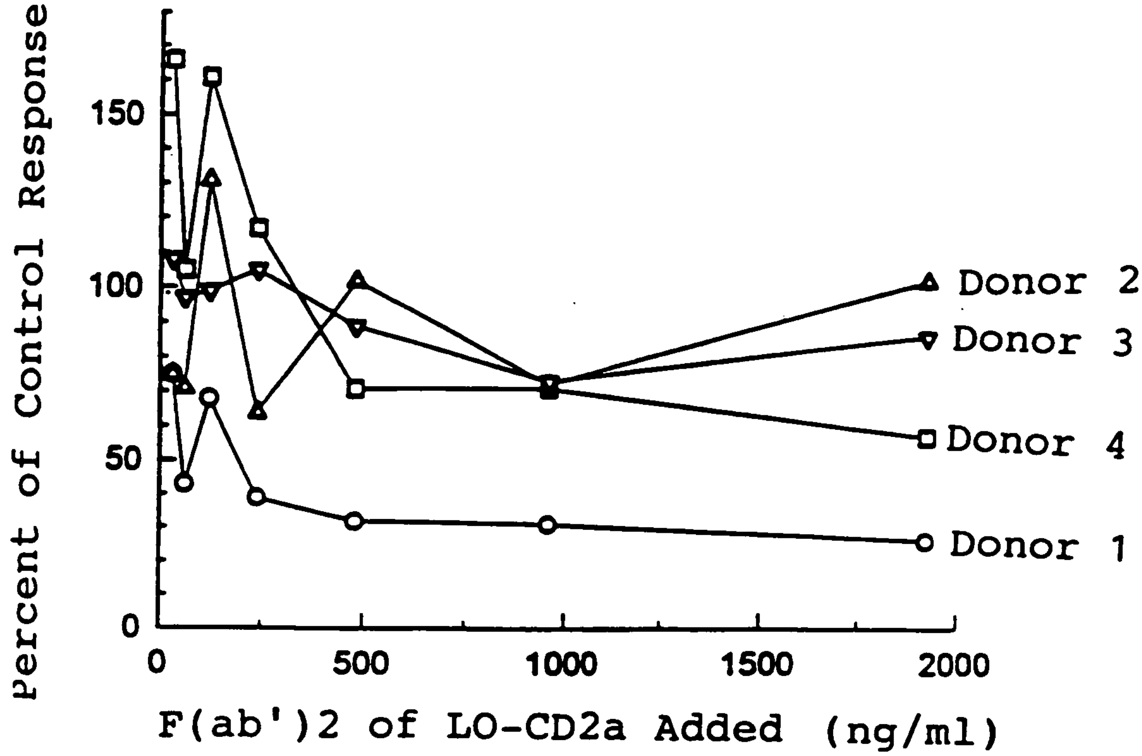

Percent of Control Response
150
100
50
0
0
500
1000
1500
2000
F(ab')2 of LO-CD2a Added (ng/ml)
Donor 2
Donor 3
Donor 4
Donor 1

FIG. 40

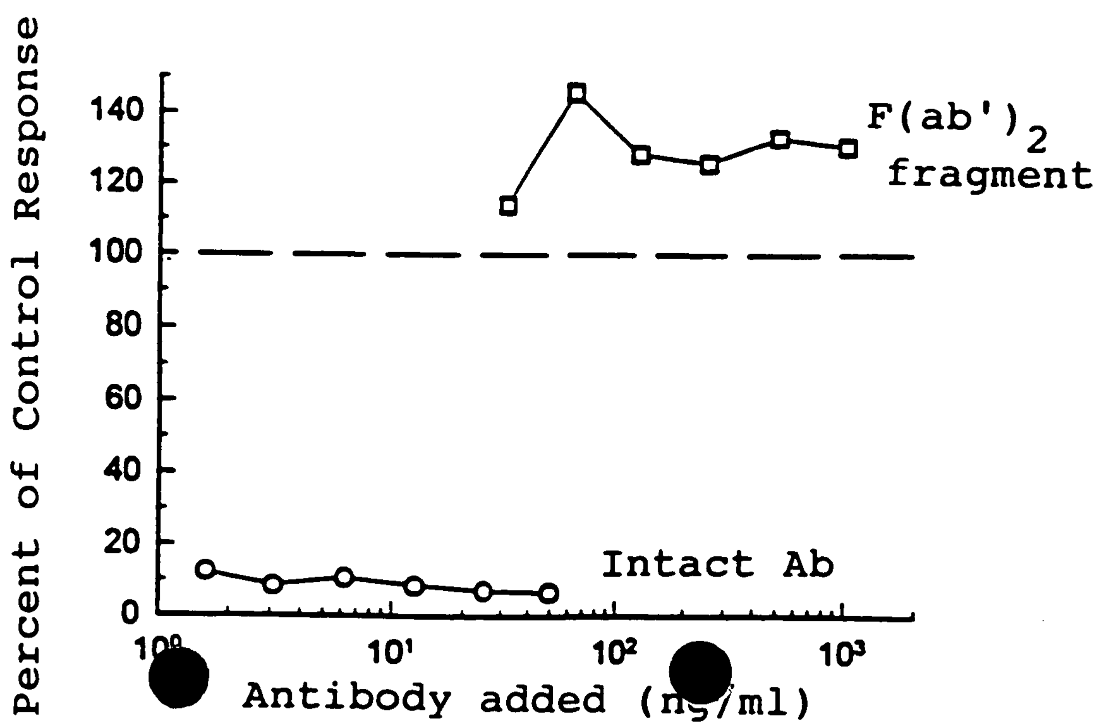

Percent of Control Response
140
120
100
80
60
40
20
0
10⁰
10¹
10²
10³
Antibody added (ng/ml)
F(ab')2 fragment
Intact Ab

FIG. 41